

sterolbiosynthesis.txt

? b biochem biosci biotech medicine

>>>W: 76 is unauthorized

44 is unauthorized

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[File 370] Science 1996-1999/Jul w3

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[File 434] SciSearch(R) Cited Ref Sci 1974-1989/Dec

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2001 (c) Action Potential. All rights reserved.

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[File 185] Zoological Record Online(R) 1864-2008/Jun

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[File 99] Wilson Appl. Sci & Tech Abs 1983-2008/Apr

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[File 266] FEDRIP 2008/Feb

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[File 358] Current BioTech Abs 1983-2006/Jan

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[File 149] TGG Health&Wellness DB(SM) 1976-2008/Jun w1

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? e au= phillips, john?

Ref	Items	Index-term
E1	2	AU=PHILLIPS, JOHN, III
E2	1	AU=PHILLIPS, JOHN, JR.
E3	0	AU=PHILLIPS, JOHN?
E4	1	AU=PHILLIPS, JOHNATHAN

```

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E5      1  AU=PHILLIPS, JOHNNY HARRIS
E6      1  AU=PHILLIPS, JOLIE
E7      8  AU=PHILLIPS, JON
E8      1  AU=PHILLIPS, JON C.
E9      1  AU=PHILLIPS, JON DOUGLAS, JR.
E10     6  AU=PHILLIPS, JON R.
E11     2  AU=PHILLIPS, JON ROWAN
E12    197 AU=PHILLIPS, JONATHAN
E13     8  AU=PHILLIPS, JONATHAN A.
E14    17  AU=PHILLIPS, JONATHAN D.
E15    48  AU=PHILLIPS, JONATHAN D.
E16     3  AU=PHILLIPS, JONATHAN DAVID
E17     3  AU=PHILLIPS, JONATHAN E.
E18     8  AU=PHILLIPS, JONATHAN E.
E19     2  AU=PHILLIPS, JONATHAN ERICK
E20     1  AU=PHILLIPS, JONATHAN FRANCIS
E21     8  AU=PHILLIPS, JONATHAN G.
E22     1  AU=PHILLIPS, JONATHAN J.
E23     1  AU=PHILLIPS, JONATHAN J.
E24     2  AU=PHILLIPS, JONATHAN M.
E25     3  AU=PHILLIPS, JONATHAN MARK
Enter PAGE for more

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? s sterol adj biosynthesis adj pathway
S1      0  S STEROL ADJ BIOSYNTHESIS ADJ PATHWAY

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? s sterol adj pathway
S2      0  S STEROL ADJ PATHWAY

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? s sterol adj biosynthesis
S3      0  S STEROL ADJ BIOSYNTHESIS

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? s cerevisiae and sterol
Processing
      587097  CEREVISIAE
      218487  STEROL
S4      6183  S CEREVISIAE AND STEROL

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? s s4 and (screen? or identif?)
Processing
Processing
Processing
      6183  S4
      2612169  SCREEN?
      9852679  IDENTIF?
S5      1356  S S4 AND (SCREEN? OR IDENTIF?)

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? s s5 and assay
      1356  S5
      2902594  ASSAY
S6      115  S S5 AND ASSAY

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? s s6 and synthesis or biosynthesis
Processing
Processing
      115  S6
      8500882  SYNTHESIS
      1723155  BIOSYNTHESIS
S7      1723163  S S6 AND SYNTHESIS OR BIOSYNTHESIS

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? s s6 and (synthesis or biosynthesis)
Processing
      115  S6

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8500882 SYNTHESIS
1723155 BIOSYNTHESIS
S8 83 S S6 AND (SYNTHESIS OR BIOSYNTHESIS)
?
rd
>>>W: Duplicate detection is not supported for File 393.
Duplicate detection is not supported for File 391.
Records from unsupported files will be retained in the RD set.
S9 38 RD (UNIQUE ITEMS)

? t s9/3,k/1-38
>>>W: KWIC option is not available in file(s): 399
9/3,k/1 (Item 1 from file: 5) Links
Fulltext available through: STIC Full Text Retrieval Options
Biosis Previews(R)
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18712687 Biosis No.: 200600058082
Characterizing sterol defect suppressors uncovers a novel transcriptional signaling
pathway regulating zymosterol biosynthesis

Author: Germann Melody (Reprint); Gallo Christina; Donahue Timothy; Shirzadi Reza;
Stukey Joseph; Lang Silvia; Ruckenstein Christoph; Oliaro-Bosso Simonetta; McDonough
Virginia; Turnowsky Friederike; Balliano Gianni; Nickels Joseph T Jr
Author Address: Drexel Univ, Coll Med, Dept Biochem and Mol Biol, Philadelphia, PA
19102 USA**USA
Journal: Journal of Biological Chemistry 280 (43): p 35904-35913 OCT 28 2005
2005
ISSN: 0021-9258
Document Type: Article
Record Type: Abstract
Language: English
Characterizing sterol defect suppressors uncovers a novel transcriptional signaling
pathway regulating zymosterol biosynthesis

Abstract: ...zymosterol. Mutant cells accumulate toxic 4-carboxysterols and are
inviable at high temperature. A genetic screen aimed at cloning recessive mutations
remediating the temperature sensitive growth defect has resulted in the... ..of
squalene and squalene epoxide, respectively. ets1-1 and ets2-1 cells accumulate
these same sterol intermediates. Chromosomal integration of ERG1 and ERG7 at their
loci in erg26-1(ts) ets1... ..that suppress the inviability of erg26-1(ts) at high
temperature, and cause accumulation of sterol intermediates and decreased enzymatic
activities. Finally using erg1-1 and erg7-1 mutant strains, we demonstrate that the
expression of the ERG25/26/27 genes required for zymosterol biosynthesis are
coordinately transcriptionally regulated, along with ERG1 and ERG7, in response to
blocks in sterol biosynthesis. Transcriptional regulation requires the transcription
factors, Upc2p and Ecm22p.

DESCRIPTORS:

Organisms: Saccharomyces cerevisiae (Ascomycetes...

Organisms: Parts Etc:

Chemicals & Biochemicals: ...biosynthesis;sterol defect suppressors

Gene Name: Saccharomyces cerevisiae ets1-1 gene (Ascomycetes... ..Saccharomyces

cerevisiae ets2-1 gene (Ascomycetes... ..Saccharomyces cerevisiae ERG1 gene

(Ascomycetes... ..Saccharomyces cerevisiae ERG7 gene (Ascomycetes...

...Saccharomyces cerevisiae ETS1 gene (Ascomycetes... ..Saccharomyces cerevisiae

ETS2 gene (Ascomycetes... ..Saccharomyces cerevisiae erg26-1ts gene (Ascomycetes)

Methods & Equipment: ...genetic screening--... ..enzymatic assay--

9/3,k/2 (Item 2 from file: 5) Links
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17690062 Biosis No.: 200400060819

Pyridines and pyrimidines mediating activity against an efflux-negative strain of *Candida albicans* through putative inhibition of lanosterol demethylase.

Author: Buurman Ed T (Reprint); Blodgett April E; Hull Kenneth G; Carcanague Daniel

Author Address: AstraZeneca R and D Boston, 35 Gatehouse Dr., Waltham, MA, 02451, USA**USA

Author E-mail Address: ed.buurman@astrazeneca.com

Journal: Antimicrobial Agents and Chemotherapy 48 (1): p 313-318 January 2004 2004

Medium: print

ISSN: 0066-4804 _(ISSN print)

Document Type: Article

Record Type: Abstract

Language: English

Abstract: The first step in ergosterol biosynthesis in *Saccharomyces cerevisiae* consists of the condensation of two acetyl coenzyme A (acetyl-CoA) moieties by acetoacetyl-CoA thiolase, encoded by ERG10. The inhibition of the sterol pathway results in feedback activation of ERG10 transcription. A cell-based reporter assay, in which increased ERG10 transcription results in elevated specific beta-galactosidase activity, was used to find novel inhibitors of ergosterol biosynthesis that could serve as chemical starting points for the development of novel antifungal agents. A class of pyridines and pyrimidines identified in this way had no detectable activity against the major fungal pathogen *Candida albicans* (MICs... ..ml-1), suggesting that they are efficiently removed from wild-type cells. Quantitative analysis of sterol intermediates that accumulated during growth inhibition revealed the accumulation of lanosterol at the expense of ergosterol. Furthermore, a clear correlation was found between the 50% inhibitory concentration at which the sterol profile was altered and the antifungal activity, measured as the MIC. This finding strongly suggests that the inhibition of growth was caused by a reduction in ergosterol synthesis. The compounds described here are a novel class of antifungal pyridines and pyrimidines and the...

DESCRIPTORS:

Organisms: *Saccharomyces cerevisiae* (Ascomycetes...

Organisms: Parts Etc:

Chemicals & Biochemicals: ...biosynthesis;

Gene Name: *Saccharomyces cerevisiae* ERG10 gene (Ascomycetes)

Methods & Equipment: cell-based reporter assay--

9/3,K/3 (Item 3 from file: 5) Links

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17651602 Biosis No.: 200400018586

Identification of two novel mutations in the murine Nsdh1 sterol dehydrogenase gene and development of a functional complementation assay in yeast.

Author: Lucas Marsha E; Ma Qi; Cunningham David; Peters Jo; Cattnach Bruce; Bard Martin; Elmore Bradley K; Herman Gail E (Reprint)

Author Address: Department of Pediatrics, Center for Molecular and Human Genetics, Columbus Children's Research Institute, 700 Children's Dr., Rm. W403, Columbus, OH, 43205, USA**USA

Author E-mail Address: hermang@pediatrics.ohio-state.edu

Journal: Molecular Genetics and Metabolism 80 (1-2): p 227-233 September-October 2003 2003

Medium: print

ISSN: 1096-7192

Document Type: Article

Record Type: Abstract

Language: English

Identification of two novel mutations in the murine Nsdh1 sterol dehydrogenase gene

sterolbiosynthesis.txt
and development of a functional complementation assay in yeast.

Abstract: ...that the mouse NSDHL protein can rescue the lethality of erg26 deficient cells of *Saccharomyces cerevisiae* that lack the yeast ortholog, substantiating the role of NSDHL as a C-3 sterol dehydrogenase. Using this in vivo assay, we have demonstrated that two Str alleles function as hypomorphs, while three Bpa and one...

DESCRIPTORS:

Chemicals & Biochemicals: ...biosynthesis
Methods & Equipment: yeast complementation assay--
Geographical Name:

9/3,K/4 (Item 4 from file: 5) Links
Fulltext available through: STIC Full Text Retrieval Options
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17509166 Biosis No.: 200300464777
Enzymological properties of sterol-C4-methyl-oxidase of yeast sterol biosynthesis.

Author: Darnet Sylvain; Rahier Alain (Reprint)
Author Address: Centre National de la Recherche Scientifique, Institut de Botanique, Institut de Biologie Moléculaire des Plantes, UPR-CNRS 2357, 28 rue Goethe, 67083, Strasbourg Cedex, France**France
Author E-mail Address: enzymo@bota-ulp.u-strasbg.fr
Journal: Biochimica et Biophysica Acta 1633 (2): p 106-117 21 July, 2003 2003
Medium: print
ISSN: 0006-3002 _(ISSN print)
Document Type: Article
Record Type: Abstract
Language: English
Enzymological properties of sterol-C4-methyl-oxidase of yeast sterol biosynthesis.

Abstract: Despite genes of the sterol methyl-oxidase component (SMO) of the sterol-C4-demethylation multienzymatic complex have been identified in a variety of organisms and the key role played by SMO in yeast sterol biosynthesis, the enzymological properties of yeast SMO have not been investigated. An enzymatic assay for measuring specifically sterol 4alpha-methyl-oxidase activity in *Saccharomyces cerevisiae* has been developed for the first time by using (14C)-4,4-dimethyl-zymosterol as... products to be characterized as well as two novel C4-hydroxymethyl-zymosterol derivatives to be identified as immediate oxidative metabolites by the yeast 4,4-dimethyl-zymosterol 4alpha-methyl-oxidase (ScSMO... low activity with 24-methylene-24-dihydrocycloartenol, the natural substrate of maize 4,4-dimethyl-sterol-C4-methyl-oxidase. Conversely, maize sterol-C4-methyl-oxidases showed extremely reduced activity with the natural substrate of ScSMO. The previously... than the maize systems. These distinct substrate specificities and inhibitor sensitivities between yeast and plant sterol -4alpha-methyl-oxidases probably reflect diversity in the structure of their active sites in relation to the distinct sterol biosynthetic pathways.

DESCRIPTORS:

Organisms: *Saccharomyces cerevisiae* {yeast} (Ascomycetes...
Organisms: Parts Etc:
Chemicals & Biochemicals: ...4,4-dimethyl-sterol-C4-methyl-oxidase...
...sterol--... biosynthesis; ... sterol-C4-methyl-oxidase...
...sterol-C4-methyl-oxidases
Methods & Equipment: enzymatic assay--
Geographical Name:
Miscellaneous Terms: Concept Codes: sterol biosynthetic pathways

9/3,K/5 (Item 5 from file: 5) Links

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16570265 Biosis No.: 200200163776

The sterol C-14 reductase encoded by the *Neurospora crassa* erg-3 gene: Essential charged and polar residues identified by site-specific mutagenesis

Author: Prakash A; Kasbekar D P (Reprint)

Author Address: Centre for Cellular and Molecular Biology, Hyderabad, 500 007, India**India

Journal: MGG Molecular Genetics and Genomics 266 (5): p 787-795 January, 2002 2002

Medium: print

ISSN: 1617-4615

Document Type: Article

Record Type: Abstract

Language: English

The sterol C-14 reductase encoded by the *Neurospora crassa* erg-3 gene: Essential charged and polar residues identified by site-specific mutagenesis

Abstract: Sterol C-14 reductase catalyses the reduction of the DELTA14,15 bond in intermediates in the sterol biosynthesis pathway using NADPH as a cofactor. We have undertaken a systematic site-directed mutational analysis of all the conserved charged and potentially proton-donating residues of the sterol C-14 reductase from *Neurospora crassa*. The effect of each mutation was determined using an in vivo assay based on the complementation of the corresponding *N. crassa* mutant (erg-3). The non-complementing...

Registry Numbers: ...sterol C-14 reductase

Enzyme Commission Number:

DESCRIPTORS:

Organisms: *Saccharomyces cerevisiae* (Ascomycetes)

Organisms: Parts Etc:

Chemicals & Biochemicals: ...sterol C-14 reductase

9/3,K/6 (Item 6 from file: 5) Links

Fulltext available through: STIC Full Text Retrieval Options
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16311037 Biosis No.: 200100482876

Mutations in the 3beta-hydroxysterol DELTA24-reductase gene cause desmosterolosis, an autosomal recessive disorder of cholesterol biosynthesis

Author: Waterham Hans R (Reprint); Koster Janet; Romeijn Gerrit Jan; Hennekam Raoul C M; Vreken Peter; Andersson Hans C; FitzPatrick David R; Kelley Richard I; Wanders Ronald J A

Author Address: Laboratory for Genetic Metabolic Diseases (F0-224), Department of Pediatrics, Emma Children's Hospital, Academic Medical Center, University of Amsterdam, 1100 DE, Amsterdam, Netherlands**Netherlands

Journal: American Journal of Human Genetics 69 (4): p 685-694 October, 2001 2001

Medium: print

ISSN: 0002-9297

Document Type: Article

Record Type: Abstract

Language: English

...in the 3beta-hydroxysterol DELTA24-reductase gene cause desmosterolosis, an autosomal recessive disorder of cholesterol biosynthesis

Abstract: ...abnormality suggests a deficiency of the enzyme 3beta-hydroxysterol DELTA24-reductase (DHCR24), which, in cholesterol biosynthesis, catalyzes the

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reduction of the DELTA24 double bond of sterol intermediates. We identified the human DHCR24 cDNA, by the similarity between the encoded protein and a recently characterized... ..enzyme-DWF1/DIM, from *Arabidopsis thaliana*-catalyzing a different but partially similar reaction in steroid/sterol biosynthesis in plants. Heterologous expression, in the yeast *Saccharomyces cerevisiae*, of the DHCR24 cDNA, followed by enzyme-activity measurements, confirmed that it encodes DHCR24. The... ..nicotinamide adenine dinucleotide phosphate and is increased twofold by the addition of FAD to the assay. The corresponding gene, DHCR24, was identified by database searching, spans approx 46.4 kb, is localized to chromosome 1p31.1-p33, and... ..the patient alleles, to be disease causing. Our data demonstrate that desmosterolosis is a cholesterol-biosynthesis disorder caused by mutations in DHCR24.

DESCRIPTORS:

Organisms: *Saccharomyces cerevisiae* {yeast} (Ascomycetes...

Organisms: Parts Etc:

Chemicals & Biochemicals: ...biosynthesis;

9/3,K/7 (Item 7 from file: 5) Links

Fulltext available through: STIC Full Text Retrieval Options

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15629228 Biosis No.: 200000347541

Functional discovery via a compendium of expression profiles

Author: Hughes Timothy R; Marton Matthew J; Jones Allan R; Roberts Christopher J; Stoughton Roland; Armour Christopher D; Bennett Holly A; Coffey Ernest; Dai Hongyue; He Yudong D; Kidd Matthew J; King Amy M; Meyer Michael R; Slade David; Lum Pek Y; Stepaniants Sergey B; Shoemaker Daniel D; Gachotte Daniel ; Chakraborty Kalpana; Simon Julian; Bard Martin; Friend Stephen H (Reprint)

Author Address: Rosetta Inpharmatics, Inc., 12040 115th Avenue N.E., Kirkland, WA, 98034, USA**USA

Journal: Cell 102 (1): p 109-126 July 7, 2000 2000

Medium: print

ISSN: 0092-8674

Document Type: Article

Record Type: Abstract

Language: English

Abstract: ...on the cell is a fundamental problem in biology. Here, we describe how a single assay can be used to monitor hundreds of different cellular functions simultaneously. We constructed a reference... ..or "compendium" of expression profiles corresponding to 300 diverse mutations and chemical treatments in *S. cerevisiae*, and we show that the cellular pathways affected can be determined by pattern matching, evenof this approach is validated by examining profiles caused by deletions of uncharacterized genes: we identify and experimentally confirm that eight uncharacterized open reading frames encode proteins required for sterol metabolism, cell wall function, mitochondrial respiration, or protein synthesis. We also show that the compendium can be used to characterize pharmacological perturbations by identifying a novel target of the commonly used drug dyclonine.

DESCRIPTORS:

Organisms: *Saccharomyces cerevisiae* (Ascomycetes)

Organisms: Parts Etc:

Miscellaneous Terms: Concept Codes: ...protein synthesis

9/3,K/8 (Item 8 from file: 5) Links

Fulltext available through: STIC Full Text Retrieval Options

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15384742 Biosis No.: 200000103055

Competition between a sterol biosynthetic enzyme and tRNA modification in addition to changes in the protein synthesis machinery causes altered nonsense suppression

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Author: Benko Ann L; Vaduva Gabriela; Martin Nancy C; Hopper Anita K (Reprint)
Author Address: Department of Biochemistry and Molecular Biology, Pennsylvania State University College of Medicine, 500 University Drive, H171, Hershey, PA, 17033, USA**USA
Journal: Proceedings of the National Academy of Sciences of the United States of America 97 (1): p 61-66 Jan. 4, 2000 2000
Medium: print
ISSN: 0027-8424
Document Type: Article
Record Type: Abstract
Language: English
Competition between a sterol biosynthetic enzyme and tRNA modification in addition to changes in the protein synthesis machinery causes altered nonsense suppression

Abstract: The *Saccharomyces cerevisiae* Mod5 protein catalyzes isopentenylation of A to i6A on tRNAs in the nucleus, cytosol, and... ..Mod5p, dimethylallyl pyrophosphate, is also a substrate for Erg20p that catalyzes an essential step in sterol biosynthesis. Changing the distribution of Mod5p so that less Mod5p is present in the cytosol decreases... ..on cytosolic tRNAs and alters tRNA-mediated nonsense suppression. We devised a colony color/growth assay to assess tRNA-mediated nonsense suppression and used it to search for genes, which, when overexpressed, affect nonsense suppression. We identified SAL6, TEF4, and YDL219w, all of which likely affect nonsense suppression via alteration of the protein synthesis machinery. We also identified ARC1, whose product interacts with aminoacyl synthetases. Interestingly, we identified ERG20. Midwestern analysis showed that yeast cells overproducing Erg20p have reduced levels of i6A on tRNAs. Thus, Erg20p appears to affect nonsense suppression by competing with Mod5p for substrate. Identification of ERG20 reveals that yeast have a limited pool of dimethylallyl pyrophosphate. It also demonstrates...

DESCRIPTORS:

Organisms: *Saccharomyces cerevisiae* (Ascomycetes)

Organisms: Parts Etc:

Chemicals & Biochemicals: ...*Saccharomyces cerevisiae*, protein... ..synthesis, synthesis machinery... ..sterol--... ..biosynthesis;*Saccharomyces cerevisiae* ARC1 gene... ..identification;*Saccharomyces cerevisiae* ERG20 gene... ..identification;*Saccharomyces cerevisiae* SAL6 gene... ..identification;*Saccharomyces cerevisiae* TEF4 gene... ..identification;*Saccharomyces cerevisiae* YDL219w gene... ..identification

9/3,K/9 (Item 9 from file: 5) Links

Fulltext available through: STIC Full Text Retrieval Options

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15004079 Biosis No.: 199900263739

Heterologous expression in *Saccharomyces cerevisiae* of an *Arabidopsis thaliana* cDNA encoding mevalonate diphosphate decarboxylase

Author: Cordier Helene (Reprint); Karst Francis; Berges Thierry
Author Address: Laboratoire de Genetique Physiologique et Moleculaire, ERS CNRS 6099, Institut de Biologie Moleculaire et d'Ingenierie Genetique, 40 Avenue du Recteur Pineau, 86 022, Poitiers Cedex, France**France
Journal: Plant Molecular Biology 39 (5): p 953-967 March, 1999 1999
Medium: print
ISSN: 0167-4412
Document Type: Article
Record Type: Abstract
Language: English
Heterologous expression in *Saccharomyces cerevisiae* of an *Arabidopsis thaliana* cDNA encoding mevalonate diphosphate decarboxylase

sterolbiosynthesis.txt

Abstract: Sequence comparison with the mevalonate diphosphate decarboxylase (MVD) amino acid sequence of *Saccharomyces cerevisiae* identified an EST clone corresponding to a cDNA that may encode *Arabidopsis thaliana* MVD (AtMVD1). This enzyme catalyses the synthesis of isopentenyl diphosphate, the building block of sterol and isoprenoid biosynthesis, and uses mevalonate diphosphate as a substrate. Sequencing of the full-length cDNA was performed... ..have at least one homologous MVD gene. In order to allow heterologous expression in *S. cerevisiae*, the MVD open reading frame (ORF) was then cloned under the control of the yeast... ..in MVD, and the lethal phenotype of an ERG19 deleted strain. However, the wild-type sterol content was not fully restored suggesting that the *A. thaliana* MVD activity may not be optimal in yeast. A two-hybrid assay was also performed to evaluate homodimer formation of the *A. thaliana* MVD and heterodimer formation...

DESCRIPTORS:

Organisms: *Saccharomyces cerevisiae* (Ascomycetes...

Organisms: Parts Etc:

9/3,K/10 (Item 10 from file: 5) Links

Fulltext available through: STIC Full Text Retrieval Options

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14996598 Biosis No.: 199900256258

Transcriptional regulation of the squalene synthase gene (ERG9) in the yeast *Saccharomyces cerevisiae*

Author: Kennedy Matthew A; Barbuch Robert; Bard Martin (Reprint)

Author Address: Department of Biology, Indiana University-Purdue University at Indianapolis, 723 W. Michigan Street, SL324, Indianapolis, IN, 46202, USA** USA

Journal: *Biochimica et Biophysica Acta* 1445 (1): p 110-122 April 14, 1999 1999

Medium: print

ISSN: 0006-3002

Document Type: Article

Record Type: Abstract

Language: English

Transcriptional regulation of the squalene synthase gene (ERG9) in the yeast *Saccharomyces cerevisiae*

Abstract: ...of the mevalonate pathway. Since the cells requirement for sterols is greater than for isoprenoids, sterol biosynthesis must be regulated independently of isoprenoid biosynthesis. In this study we explored the transcriptional regulation of squalene synthase (ERG9) in *Saccharomyces cerevisiae*, the first enzyme dedicated to the synthesis of sterols. A mutant search was performed to identify genes that were involved in the regulation of the expression of an ERG9-lacZ promoter fusion. Mutants with phenotypes consistent with known sterol biosynthetic mutations (ERG3, ERG7, ERG24) increased expression of ERG9. In addition, treatment of wild-type cells with the sterol inhibitors zaragozic acid and ketoconazole, which target squalene synthase and the C-142 sterol demethylase respectively, also caused an increase in ERG9 expression. The data also demonstrate that heme... ..several diverse factors, consistent with the idea that as the first step dedicated to the synthesis of sterols, squalene synthase gene expression and ultimately sterol biosynthesis is highly regulated.

DESCRIPTORS:

Chemicals & Biochemicals: *Saccharomyces cerevisiae* ERG9 gene {*Saccharomyces cerevisiae* squalene synthase gene...

Methods & Equipment: beta-galactosidase assay--

Geographical Name:

9/3,K/11 (Item 11 from file: 5) Links

Fulltext available through: STIC Full Text Retrieval Options

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sterolbiosynthesis.txt

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14701847 Biosis No.: 199800496094

Characterization of two human genes encoding acyl coenzyme A:cholesterol
acyltransferase-related enzymes

Author: Oelkers Peter; Behari Ajay; Cromley Debra; Billheimer Jeffrey T; Sturley
Stephen L (Reprint)

Author Address: Inst. Hum. Nutrition, Columbia Univ. Coll. Physicians Surgeons, 650
W. 168th St., New York, NY 10032, USA**USA

Journal: Journal of Biological Chemistry 273 (41): p 26765-26771 Oct. 9, 1998
1998

Medium: print

ISSN: 0021-9258

Document Type: Article

Record Type: Abstract

Language: English

Abstract: The enzyme acyl coenzyme A:cholesterol acyltransferase 1 (ACAT1) mediates
sterol esterification, a crucial component of intracellular lipid homeostasis. Two
enzymes catalyze this activity in *Saccharomyces cerevisiae* (yeast), and several
lines of evidence suggest multigene families may also exist in mammals. Using the
human ACAT1 sequence to screen data bases of expressed sequence tags, we identified
two novel and distinct partial human cDNAs. Full-length cDNA clones for these ACAT
related... ..microsomal assays in a yeast strain deleted for both esterification
genes and completely deficient in sterol esterification indicated that ARGP2
esterified cholesterol while ARGP1 did not. In contrast to ACAT1 and... ..was
relatively resistant to a histidine active site modifier. ARGP2 is therefore a
tissue-specific sterol esterification enzyme which we thus designated ACAT2. We
speculate that ARGP1 participates in the coenzymea predicted diacylglycerol
binding motif suggesting that it may perform the last acylation in triglyceride
biosynthesis.

DESCRIPTORS:

Organisms: *Saccharomyces-cerevisiae* {yeast} (Ascomycetes...

Organisms: Parts Etc:

Methods & Equipment: in vitro activity assay--... ..in vitro microsomal assay:
analysis/characterization techniquesHepG2 cDNA library hybridization
screening--

Geographical Name:

Miscellaneous Terms: Concept Codes: sterol esterification... ..triglyceride
biosynthesis

9/3,K/12 (Item 12 from file: 5) Links

Fulltext available through: STIC Full Text Retrieval Options

Biosis Previews(R)

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14238782 Biosis No.: 199800033029

A reporter gene assay for fungal sterol biosynthesis inhibitors

Author: Dixon Graham; Scanlon David; Cooper Simon; Broad Peter (Reprint)

Author Address: Lead Discovery Dep., Zeneca Pharmaceuticals, Mereside, Alderley
Park, Macclesfield, Cheshire SK10 4TG, UK**UK

Journal: Journal of Steroid Biochemistry and Molecular Biology 62 (2-3): p
165-171 June, 1997 1997

Medium: print

ISSN: 0960-0760

Document Type: Article

Record Type: Abstract

Language: English

A reporter gene assay for fungal sterol biosynthesis inhibitors

Abstract: ...thiolase (ACoAT) catalyses the condensation of two acetyl-CoA

sterolbiosynthesis.txt

molecules, the first step in the sterol biosynthetic pathway. We constructed a yeast strain containing a fusion of the promoter of the *Saccharomyces cerevisiae* ACoAT gene to a reporter gene (*Escherichia coli* beta-galactosidase). Reporter gene activity in this strain can be induced by a variety of inhibitors of sterol biosynthesis. These results suggest that the ACoAT gene is feedback regulated at the transcriptional level by products of the sterol biosynthetic pathway. The reporter gene approach described here may be used to screen chemical collections for compounds which inhibit fungal sterol biosynthesis.

DESCRIPTORS:

Organisms: *Saccharomyces-cerevisiae* (Ascomycetes...

Organisms: Parts Etc:

Chemicals & Biochemicals: ...fungal sterol biosynthesis inhibitors

Methods & Equipment: reporter gene assay--

Geographical Name:

Miscellaneous Terms: Concept Codes: sterol biosynthetic pathway...

9/3,K/13 (Item 13 from file: 5) Links

Fulltext available through: STIC Full Text Retrieval Options

Biosis Previews(R)

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13163360 Biosis No.: 199698631193

Purification and reconstitution of activity of *Saccharomyces cerevisiae* P450 61, a sterol DELTA-22-desaturase

Author: Kelly Steven L (Reprint); Lamb David C; Corran Andrew J; Baldwin Brian C; Parks Leo W; Kelly Diane E

Author Address: Krebs Inst. Biomolecular Res., Dep. Molecular Biol. Biotechnology, Sheffield Univ., Sheffield S10 2UH, UK**UK

Journal: FEBS Letters 377 (2): p 217-220 1995 1995

ISSN: 0014-5793

Document Type: Article

Record Type: Abstract

Language: English

Purification and reconstitution of activity of *Saccharomyces cerevisiae* P450 61, a sterol DELTA-22-desaturase

Abstract: P450 was purified from microsomal fractions of a strain of *Saccharomyces cerevisiae* which contained detectable P450 despite the disruption of CYP51A1. The P450 had a molecular mass of 58 kDa, similar to P4505IA1, and in an assay with rabbit NADPH-P450 reductase and dilauryl phosphatidylcholine exhibited activity for conversion of ergosta-5of the purified protein corresponded to the translated sequence of P450 61 which was recently identified during sequencing of chromosome XIII. This allowed the function of this family of P450 to be identified as sterol DELTA-22-desaturation in the pathway of ergosterol biosynthesis.

DESCRIPTORS:

Organisms: *Saccharomyces cerevisiae* (Ascomycetes)

Organisms: Parts Etc:

Miscellaneous Terms: Concept Codes: ...ERGOSTEROL BIOSYNTHESIS; ...
...STEROL-22-DESATURASE ACTIVITY

9/3,K/14 (Item 1 from file: 24) Links

Fulltext available through: STIC Full Text Retrieval Options

CSA Life Sciences Abstracts

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0002285395 IP Accession No: 5315726

Mutations in the 3 beta -Hydroxysterol Delta super(24)-Reductase Gene Cause Desmosterolosis, an Autosomal Recessive Disorder of Cholesterol Biosynthesis

Waterham, HR; Koster, J; Romeijn, GJ; Hennekam, RCM; Vreken, P; Andersson, HC;

sterolbiosynthesis.txt

Patrick, DRF; Kelley, RI; Wanders, RJA Departments of Pediatrics and Clinical Chemistry, Emma Children's Hospital, Academic Medical Center, University of Amsterdam, Amsterdam
American Journal of Human Genetics , v 69 , n 4 , p 685-694 , October 2001
Publication Date: 2001

Document Type: Journal Article

Record Type: Abstract

Language: English

Summary Language: English

ISSN: 0002-9297

File Segment: Genetics Abstracts

...beta -Hydroxysterol Delta super(24)-Reductase Gene Cause Desmosterolosis, an Autosomal Recessive Disorder of Cholesterol Biosynthesis

Abstract:

...deficiency of the enzyme 3 beta -hydroxysterol Delta super(24)-reductase (DHCR24), which, in cholesterol biosynthesis, catalyzes the reduction of the Delta super(24) double bond of sterol intermediates. We identified the human DHCR24 cDNA, by the similarity between the encoded protein and a recently characterized...
...enzyme--DWF1/DIM, from Arabidopsis thaliana--catalyzing a different but partially similar reaction in steroid/sterol biosynthesis in plants. Heterologous expression, in the yeast Saccharomyces cerevisiae, of the DHCR24 cDNA, followed by enzyme-activity measurements, confirmed that it encodes DHCR24. The...
...nicotinamide adenine dinucleotide phosphate and is increased twofold by the addition of FAD to the assay. The corresponding gene, DHCR24, was identified by database searching, spans similar to 46.4 kb, is localized to chromosome 1p31.1...
...the patient alleles, to be disease causing. Our data demonstrate that desmosterolosis is a cholesterol-biosynthesis disorder caused by mutations in DHCR24.

9/3,K/15 (Item 2 from file: 24) Links

Fulltext available through: STIC Full Text Retrieval Options

CSA Life Sciences Abstracts

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0001682392 IP Accession No: 4000108

Purification and reconstitution of activity of Saccharomyces cerevisiae P450 61, a sterol Delta super(22)-desaturase

Kelly, SL; Lamb, DC; Corran, AJ; Baldwin, BC; Parks, LW; Kelly, DE Krebs Inst. for Biomolecular Res., Dep. Mol. Biol. and Biotechnol., Sheffield Univ., Sheffield S10 2UH, UK

FEBS Letters , v 377 , n 2 , p 217-220 , December 1995

Publication Date: 1995

Document Type: Journal Article

Record Type: Abstract

Language: English

Summary Language: English

ISSN: 0014-5793

File Segment: Algology, Mycology & Protozoology Abstracts (Microbiology C)

Purification and reconstitution of activity of Saccharomyces cerevisiae P450 61, a sterol Delta super(22)-desaturase

Abstract:

P450 was purified from microsomal fractions of a strain of Saccharomyces cerevisiae which contained detectable P450 despite the disruption of CYP51A1. The P450 had a molecular mass of 58 kDa, similar to P450 51A1, and in a reconstituted assay with rabbit NADPH-P450 reductase and dilauryl phosphatidylcholine exhibited activity for

sterolbiosynthesis.txt

conversion of ergosta-5of the purified protein corresponded to the translated sequence of P450 61 which was recently identified during sequencing of chromosome XIII. This allowed the function of this family of P450 to be identified as sterol Delta super(22)-desaturation in the pathway of ergosterol biosynthesis.

Descriptors: *Saccharomyces cerevisiae*

Identifiers: cytochrome P450 61; desaturase; sterol Delta super(22)-desaturase

9/3,K/16 (Item 3 from file: 24) Links

Fulltext available through: STIC Full Text Retrieval Options

CSA Life Sciences Abstracts

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0000666166 IP Accession No: 1729240

Paxisterol, a new analgesic sterol without antiinflammation activity from *Penicillium* .

Nakano, H; Hara, M; Yamashita, Y; Ando, K; Shuto, K Tokyo Res. Lab., Kyowa Hakko Kogyo Co., Ltd., Machida, Tokyo, Japan

Journal of Antibiotics , v 41 , n 3 , p 409-410 , 1988

Addl. Source Info: Journal of Antibiotics [J. ANTIBIOT.], vol. 41, no. 3, pp. 409-410, 1988

Publication Date: 1988

Document Type: Journal Article

Record Type: Abstract

Language: English

ISSN: 0021-8820

File Segment: Biotechnology Research Abstracts; Algology, Mycology & Protozoology Abstracts (Microbiology C); Industrial & Applied Microbiology Abstracts (Microbiology A)

Paxisterol, a new analgesic sterol without antiinflammation activity from *Penicillium* .

Abstract:

The authors have screened fungi isolated from soils and plants for their ability to produce new steroids which inhibit growth of a strain of *Saccharomyces cerevisiae* in a medium without supplement of ergosterol. They now have isolated a new sterol from a culture broth of a *Penicillium* and found that this new sterol, named paxisterol, has analgesic activity in the mouse ACOH writhing assay. In contrast to corticosteroid, paxisterol does not have antiinflammatory activity. These results suggest that paxisterol is a new class of analgesic sterol and is of interest to use in modifying pain which has been difficult to relieve.

Identifiers: soil isolates; biosynthesis; *Penicillium paxilli*; paxisterol

Subj Catg:

9/3,K/17 (Item 1 from file: 34) Links

Fulltext available through: STIC Full Text Retrieval Options

SciSearch(R) Cited Ref Sci

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11396005 Genuine Article#: 647BJ No. References: 40

Evidence for multiple sterol methyl transferase pathways in *Pneumocystis carinii*

Author: Zhou WX; Nguyen TTM; Collins MS; Cushion MT; Nes WD (REPRINT)

Corporate Source: Texas Tech Univ, Dept Chem & Biochem, Lubbock//TX/79409 (REPRINT);

Texas Tech Univ, Dept Chem & Biochem, Lubbock//TX/79409; Univ Cincinnati, Coll Med,

Dept Internal Med, Cincinnati//OH/45267; Vet Adm Med Ctr, Cincinnati//OH/

Journal: LIPIDS , 2002 , v 37 , n12 (DEC) , p 1177-1186

ISSN: 0024-4201 Publication date: 20021200

Publisher: AMER OIL CHEMISTS SOC A O C S PRESS , 1608 BROADMOOR DRIVE, CHAMPAIGN, IL

sterolbiosynthesis.txt

61821-0489 USA

Language: English Document Type: ARTICLE (ABSTRACT AVAILABLE)

Evidence for multiple sterol methyl transferase pathways in *Pneumocystis carinii*

Abstract: The sterol composition of *Pneumocystis carinii*, an opportunistic pathogen responsible for life-threatening pneumonia in immunocompromised patients, was determined. Our purpose was to identify pathway-specific enzymes to impair using sterol biosynthesis inhibitors. Prior to this study, cholesterol 15 (ca. 80% of total sterols), lanosterol 1, and... ..from *P. carinii* by culturing the microorganism in steroid-immunosuppressed rats. Thirty-one sterols were identified from the fungus (total sterol = 100 fg/cell), and seven sterols were identified from rat chow. Unusual sterols in the fungus not present in the diet included, 24... ..12; and 24beta-methylcholesterol 13. The structural, relationships of the 24-alkyl groups in the sterol side chain were demonstrated chromatographically relative to authentic specimens, by MS and high-resolution H... ..4, 1 --> 2 --> 5 --> 8 --> 7. Formation of 3 is considered to form an interrupted sterol pathway. Taken together, operation of distinct sterol methyl transferase (SMT) pathways that generate 24beta-alkyl sterols in *P. carinii* with no counterpart...
Identifiers-- ...SACCHAROMYCES-CEREVISIAE; BIOSYNTHESIS; METHYLTRANSFERASE; DELTA(24(25)); SPECIFICITY; EVOLUTION; AGENTS; ENZYME; ASSAY

9/3,K/18 (Item 2 from file: 34) Links

Fulltext available through: STIC Full Text Retrieval Options

SciSearch(R) Cited Ref Sci

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07772319 Genuine Article#: 206XC No. References: 33

Identification, characterization, and partial purification of 4
alpha-carboxysterol-C3-dehydrogenase/C4-decarboxylase from *Zea mays*

Author: Rondet S; Taton M; Rahier A (REPRINT)

Corporate Source: INST BIOL MOL PLANTES,DEPT ENZYMOL MOL & CELLULAIRE, CNRS, UPR 406, 28 RUE GOETHE/F-67083 STRASBOURG//FRANCE/ (REPRINT); INST BIOL MOL PLANTES,DEPT ENZYMOL MOL & CELLULAIRE, CNRS, UPR 406/F-67083 STRASBOURG//FRANCE/
Journal: ARCHIVES OF BIOCHEMISTRY AND BIOPHYSICS , 1999 , V 366 , N2 (JUN 15) , P 249-260

ISSN: 0003-9861 Publication date: 19990615

Publisher: ACADEMIC PRESS INC , 525 B ST, STE 1900, SAN DIEGO, CA 92101-4495

Language: English Document Type: ARTICLE (ABSTRACT AVAILABLE)

Identification, characterization, and partial purification of 4
alpha-carboxysterol-C3-dehydrogenase/C4-decarboxylase from *Zea mays*

Abstract: ...the first in vitro evidence for this enzymatic activity in a higher plant. A GC assay has been developed to detect the Delta(7)-cholestenone produced and the kinetic parameters of...

Identifiers-- ...PLANT STEROL BIOSYNTHESIS; CHOLESTEROL-BIOSYNTHESIS ; OBTUSIFOLIOL 14-ALPHA-DEMETHYLASE; SACCHAROMYCES-CEREVISIAE; LANOSTEROL; SOLUBILIZATION; DEMETHYLATION; DECARBOXYLASE; INTERMEDIATE; 14-REDUCTASE

9/3,K/19 (Item 3 from file: 34) Links

Fulltext available through: STIC Full Text Retrieval Options

SciSearch(R) Cited Ref Sci

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04999387 Genuine Article#: UY930 No. References: 61

PURIFICATION, MOLECULAR-CLONING, AND EXPRESSION OF THE MAMMALIAN SIGMA(1)-BINDING SITE

Author: HANNER M; MOEBIUS FF; FLANDORFER A; KNAUS HG; STRIESSNIG J; KEMPNER E; GLOSSMANN H

Corporate Source: INNSBRUCK UNIV,INST BIOCHEM PHARMAKOL,PETER MAYR STR 1/A-6020 INNSBRUCK//AUSTRIA/; INNSBRUCK UNIV,INST BIOCHEM PHARMAKOL/A-6020 INNSBRUCK//AUSTRIA/; NIAMSD,NIH/BETHESDA//MD/20892

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Journal: PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA , 1996 , V 93 , N15 (JUL 23) , P 8072-8077
ISSN: 0027-8424

Language: ENGLISH Document Type: ARTICLE (Abstract Available)

Abstract: ...of 24 +/- 2 kDa, The corresponding cDNA was cloned using degenerate oligonucleotides and cDNA library screening, Its open reading frame encoded a 25.3-kDa protein with at least one putative... ..structurally unrelated to known mammalian proteins but it shared homology with fungal proteins involved in sterol synthesis, Northern blots showed high densities of the sigma(1)-binding site mRNA in sterol-producing tissues, This is also in agreement with the known ability of sigma(1)-binding...

Identifiers-- ...C-8 STEROL ISOMERASE; GUINEA-PIG LIVER; RADIATION INACTIVATION; SIGMA-RECEPTORS; CHOLESTEROL-BIOSYNTHESIS; ENDOPLASMIC-RETICULUM; RAT-LIVER; BINDING POLYPEPTIDE; H-3 (+)-PENTAZOCINE; MICROSOMAL-ENZYMES

Research Fronts: ...OPIOID RECEPTOR MESSENGER-RNA DISTRIBUTION; FUNCTIONAL EXPRESSION; SYSTEMICALLY ADMINISTERED NOR-BINALTORPHIMINE IN A THERMAL ANTINOCICEPTION ASSAY)

94-3070 001 (RAT SKELETAL-MUSCLE; DEVELOPMENTAL REGULATION; YEAST SACCHAROMYCES-CEREVISIAE)

Cited References:

9/3,K/20 (Item 4 from file: 34) Links

Fulltext available through: STIC Full Text Retrieval Options

SciSearch(R) Cited Ref Sci

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03332048 Genuine Article#: NX107 No. References: 27

PLANT STEROL BIOSYNTHESIS - IDENTIFICATION OF A NADPH DEPENDENT STERONE REDUCTASE INVOLVED IN STEROL-4 DEMETHYLATION

Author: PASCAL S; TATON M; RAHIER A

Corporate Source: INST BOT,INST BIOL MOLEC PLANTES,DEPT ENZYMOL CELLULAIRE & MOLEC,CNRS,UPR 406,28 RUE GOETHE/F-67083 STRASBOURG//FRANCE/; INST BOT,INST BIOL MOLEC PLANTES,DEPT ENZYMOL CELLULAIRE & MOLEC,CNRS,UPR 406/F-67083 STRASBOURG//FRANCE/

Journal: ARCHIVES OF BIOCHEMISTRY AND BIOPHYSICS , 1994 , V 312 , N1 (JUL) , P 260-271

ISSN: 0003-9861

Language: ENGLISH Document Type: ARTICLE (Abstract Available)

PLANT STEROL BIOSYNTHESIS - IDENTIFICATION OF A NADPH DEPENDENT STERONE REDUCTASE INVOLVED IN STEROL-4 DEMETHYLATION

Abstract: ...the reduction of various sterones to produce stereoselectively the corresponding 3 beta-hydroxy derivatives. Enzymatic assay conditions have been developed to characterize this reduction step and the kinetics of the microsomal... ..or C-31-sterones react poorly. The results support the conclusion that the reductase activity identified is a constitutive component of the microsomal sterol 4-demethylation complex recently identified in photosynthetic organisms (S. Pascal et al., 1993, J. Biol. Chem. 268, 11639). They are...

Identifiers-- ...STRUCTURAL REQUIREMENTS; SACCHAROMYCES-CEREVISIAE;

MEMBRANE-FUNCTION; PURIFICATION; SUBSTRATE; CLEAVAGE; CULTURES; LIVER; MAIZE

Research Fronts: ...3-ALPHA-HYDROXYSTEROID DEHYDROGENASE; CARBONYL REDUCTASE; BOVINE LIVER CYTOSOL; ASYMMETRIC MICROBIAL REDUCTION)

92-2772 001 (STEROL BIOSYNTHESIS; MEMBRANE CHOLESTEROL; PROKARYOTIC TRITERPENOIDS OF THE HOPANE SERIES; CYANOBACTERIUM SYNECHOCYSTIS PCC-6714; ORIENTED BILAYERS)

Cited References:

9/3,K/21 (Item 5 from file: 34) Links

Fulltext available through: STIC Full Text Retrieval Options

SciSearch(R) Cited Ref Sci

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02930969 Genuine Article#: MT183 No. References: 29

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DEVELOPMENT OF A CELL-FREE ASSAY FROM BOTRYTIS-CINEREA AS A BIOCHEMICAL SCREEN FOR STEROL BIOSYNTHESIS INHIBITORS

Author: STEHMANN C; KAPTEYN JC; DEWAARD MA

Corporate Source: WAGENINGEN UNIV AGR,DEPT PHYTOPATHOL,POB 8025/6700 EE
WAGENINGEN//NETHERLANDS/; WAGENINGEN UNIV AGR,DEPT PHYTOPATHOL,POB 8025/6700 EE
WAGENINGEN//NETHERLANDS/

Journal: PESTICIDE SCIENCE , 1994 , V 40 , N1 (JAN) , P 1-8

ISSN: 0031-613X

Language: ENGLISH Document Type: ARTICLE (Abstract Available)

DEVELOPMENT OF A CELL-FREE ASSAY FROM BOTRYTIS-CINEREA AS A BIOCHEMICAL SCREEN FOR STEROL BIOSYNTHESIS INHIBITORS

Abstract: An assay for measuring ergosterol synthesis in cell-free extracts of the filamentous plant pathogen *Botrytis cinerea* is described. The extracts... ..by mechanical disruption of young conidial germlings in a Bead-Beater apparatus. The C4-desmethyl sterol fraction consisted of three distinct compounds and totalled 39% of the non-saponifiable lipids formedlanosterol (54%) and eburicol (28%). The cell-free system had a narrow pH optimum for synthesis of C4-desmethyl sterols of pH 7.3-7.4. Cell-free synthesis of C4-desmethyl sterols was inhibited by the imidazole fungicide imazalil, concomitant with an accumulation of eburicol. The IC50 value (concentration of fungicide which inhibited cell-free synthesis of C4-desmethyl sterols by 50%) was 9.1×10^{-9} M. These results... ..consistent with the hypothesis that imazalil is a potent inhibitor of the cytochrome P450-dependent sterol 14 α -demethylase of *B. cinerea*. The method described may be used to screen compounds biochemically for inhibition of sterol synthesis in an agriculturally important plant pathogen.

Identifiers-- ...CANDIDA-ALBICANS; ERGOSTEROL BIOSYNTHESIS; SACCHAROMYCES-CEREVISIAE; S-ADENOSYLMETHIONINE; METHYLTRANSFERASE; FUNGICIDES; MECHANISM; LOCATION

Research Fronts: 92-0453 001 (STEROL BIOSYNTHESIS INHIBITORS; BINDING CONFORMATION OF TERTIARY AMINE FUNGICIDES; ERGOSTEROL SYNTHESIS)

Cited References:

9/3,K/22 (Item 6 from file: 34) Links

Fulltext available through: STIC Full Text Retrieval Options

SciSearch(R) Cited Ref Sci

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02014716 Genuine Article#: JU104 No. References: 25

DESIGN OF STEROL REDUCTASE INHIBITORS - INSIGHTS INTO THE BINDING CONFORMATION OF TERTIARY AMINE FUNGICIDES

Author: BASARAB GS; LIVINGSTON RS; VOLLMER SJ; JOHNSON CB; KRANIS KT

Corporate Source: DUPONT CO,AGR PROD,STINE HASKELL RES CTR,BLDG 300/NEWARK//DE/19714

Journal: ACS SYMPOSIUM SERIES , 1992 , V 504 , P 414-427

ISSN: 0097-6156

Language: ENGLISH Document Type: REVIEW (Abstract Available)

DESIGN OF STEROL REDUCTASE INHIBITORS - INSIGHTS INTO THE BINDING CONFORMATION OF TERTIARY AMINE FUNGICIDES

Abstract: The data presented suggest that the binding conformation of tertiary amine fungicides to DELTA8,14-sterol reductase in fungi correlates with a pseudo-1,3-diequatorial orientation of the amine moiety and a lipophilic group around a cyclopentane. This NADPH dependent enzyme reduces a D-ring sterol double bond through a presumed transition state carbocation which the protonated amine inhibitors are thought to mimic. We designed conformationally restricted tertiary amines based on the sterol D-ring framework and evaluated inhibition of the reductase enzyme in a microsomal assay developed from *Saccharomyces cerevisiae*. Identified was 1-[5-[4-(1,1-dimethylethyl)-phenyl]-1-methyl-6-oxabicyclo[3.1.0... Identifiers-- ...SACCHAROMYCES-CEREVISIAE; ERGOSTEROL BIOSYNTHESIS; FENPROPIMORPH; DELTA-14-REDUCTASE; TRIDEMORPH

sterolbiosynthesis.txt

9/3,K/23 (Item 7 from file: 34) Links

SciSearch(R) Cited Ref Sci

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01856861 Genuine Article#: JG848 No. References: 30

ENZYME-SYSTEMS - USE IN THE DEVELOPMENT OF STEROL BIOSYNTHESIS INHIBITORS AS AGROCHEMICALS

Author: MERCER EI

Corporate Source: UNIV COLL ABERYSTWYTH,DEPT BIOCHEM/ABERYSTWYTH SY23

3DD/DYFED/WALES/

Journal: ACS SYMPOSIUM SERIES , 1992 , V 497 , P 162-173

Language: ENGLISH Document Type: REVIEW (Abstract Available)

ENZYME-SYSTEMS - USE IN THE DEVELOPMENT OF STEROL BIOSYNTHESIS INHIBITORS AS AGROCHEMICALS

Abstract: Although the sterol biosynthesis inhibitors currently in use as agrochemicals were discovered by classical screening procedures, it is now clear that the development of new ones can be facilitated by... ..the efficacy of candidate compounds as inhibitors of the particular target enzyme. This paper describes assay procedures, based upon enzyme preparations derived from a high sterol strain of *Saccharomyces cerevisiae*, for comparing the efficacy of compounds as inhibitors of squalene epoxidase, 2,3-epoxysqualene:lanosterol cyclase, sterol 14-demethylase, sterol 4-demethylase, sterol DELTA-14-reductase and sterol DELTA-8--> DELTA-7-isomerase.

Identifiers-- ...SACCHAROMYCES-CEREVISIAE; SQUALENE EPOXIDASE; CUCURBITA-MAXIMA; CANDIDA-ALBICANS; PACLOBUTRAZOL; FENPROPIMORPH; TRIDEMORPH

Research Fronts: 90-2365 002 (ABSCISIC-ACID BIOSYNTHESIS; VEGETATIVE GROWTH; MARINE LIPIDS; TRANSLOCATION OF UNICONAZOLE; GIBBERELLIN-STEROL INHIBITORS; BAS111 IN APPLE SEEDLINGS)

Cited References:

9/3,K/24 (Item 8 from file: 34) Links

SciSearch(R) Cited Ref Sci

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00957468 Genuine Article#: FJ040 No. References: 87

FUNGAL-INFECTIONS AND THEIR MANAGEMENT

Author: GRAYBILL JR; SHARKEY PK

Corporate Source: UNIV TEXAS,HLTH SCI CTR/SAN ANTONIO//TX/78284

Journal: BRITISH JOURNAL OF CLINICAL PRACTICE , 1990 , V 44 , N9 , P 23-31

Language: ENGLISH Document Type: ARTICLE (Abstract Available)

Abstract: ...but it was soon appreciated that high doses caused impairment of testosterone and ultimately cortisol synthesis. Dose-dependent nausea and vomiting also became apparent, as did the necessity for very high...

Identifiers--

Research Fronts: ...THERAPY; CHRONIC SYSTEMIC CANDIDIASIS; IMMUNOCOMPROMISED HOST; INFECTION IN NEUTROPENIC PATIENTS)

89-3046 003 (DISSEMINATED HISTOPLASMOSIS; ASSAY OF FLUCONAZOLE; SYSTEMIC MYCOSES; PULMONARY BLASTOMYCOSIS DURING KETOCONAZOLE THERAPY; INVITRO ANTIFUNGAL ACTIVITY)

89-3740 003 (HIGH-DOSE KETOCONAZOLE THERAPY; ESTROGEN BIOSYNTHESIS; AROMATASE INHIBITORS; VAGINAL CANDIDIASIS)

89-2270 002 (MURINE CRYPTOCOCCOSIS; INVITRO ACTIVITY OF CILOFUNGIN (LY121019); PULMONARY INFECTIONS IN THE ACQUIRED IMMUNE-DEFICIENCY SYNDROME; ANTIFUNGAL AGENTS)

89-2740 001 (STEROL BIOSYNTHESIS; YEAST SACCHAROMYCES-CEREVISIAE; IMIDAZOLE DRUGS INCLUDING KETOCONAZOLE)

89-6242 001 (DISSEMINATED TRICHOSPORON BEIGELII INFECTION; IMMUNOHISTOCHEMICAL IDENTIFICATION OF FUNGAL ELEMENTS; NEUTROPENIC PATIENT)

Cited References:

9/3,K/25 (Item 1 from file: 71) Links

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01852934 2001211007

Mutations in the 3beta-hydroxysterol DELTASUP24-reductase gene cause desmosterolosis, an autosomal recessive disorder of cholesterol biosynthesis

Waterham H.R.; Koster J.; Romeijn G.J.; Hennekam R.C.M.; Vreken P.; Andersson H.C.; FitzPatrick D.R.; Kelley R.I.; Wanders R.J.A.

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Email: h.r.waterham@amc.uva.nl

Journal : American Journal of Human Genetics, 69/4 (685-694), 2001, United States

CODEN: AJHGA

ISSN: 0002-9297

Document Type: Article

Languages: English Summary Languages: English

No. of References: 43

...in the 3beta-hydroxysterol DELTASUP24-reductase gene cause desmosterolosis, an autosomal recessive disorder of cholesterol biosynthesis

...abnormality suggests a deficiency of the enzyme 3beta-hydroxysterol DELTASUP24-reductase (DHCR24), which, in cholesterol biosynthesis, catalyzes the reduction of the DELTASUP24 double bond of sterol intermediates. We identified the human DHCR24 cDNA, by the similarity between the encoded protein and a recently characterized... enzyme - DWFL1/ DIM, from Arabidopsis thaliana - catalyzing a different but partially similar reaction in steroid/sterol biosynthesis in plants. Heterologous expression, in the yeast Saccharomyces cerevisiae, of the DHCR24 cDNA, followed by enzyme-activity measurements, confirmed that it encodes DHCR24. The... nicotinamide adenine dinucleotide phosphate and is increased twofold by the addition of FAD to the assay. The corresponding gene, DHCR24, was identified by database searching, spans (similar)46.4 kb, is localized to chromosome 1p31.1-p33... the patient alleles, to be disease causing. Our data demonstrate that desmosterolosis is a cholesterol-biosynthesis disorder caused by mutations in DHCR24.

9/3,K/26 (Item 2 from file: 71) Links

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00350845 96014328

Purification and reconstitution of activity of Saccharomyces cerevisiae P450 61, a sterol Deltasup 2sup 2-desaturase

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Address: S.L. Kelly, Krebs Inst Biomolecular Research, Department Molecular Biol/Biotechnol, Sheffield University, Sheffield S10 2UH, United Kingdom

Journal : FEBS Letters, 377/2 (217-220), 1995, Netherlands

PUBLICATION DATE: 19950000

CODEN: FEBLA

ISSN: 0014-5793

Document Type: Article

Languages: English Summary Languages: English

Purification and reconstitution of activity of Saccharomyces cerevisiae P450 61, a sterol Deltasup 2sup 2-desaturase

P450 was purified from microsomal fractions of a strain of Saccharomyces cerevisiae which contained detectable P450 despite the disruption of CYP51A1. The P450 had a

sterolbiosynthesis.txt

molecular mass of 58 kDa, similar to P450 51A1, and in a reconstituted assay with rabbit NADPH-P450 reductase and dilauryl phosphatidylcholine exhibited activity for conversion of ergosta-5of the purified protein corresponded to the translated sequence of P450 61 which was recently identified during sequencing of chromosome XIII. This allowed the function of this family of P450 to be identified as sterol Deltasup 2sup 2-desaturation in the pathway of ergosterol biosynthesis.

DESCRIPTORS:

Sterol Deltasup 2sup 2-desaturase; Purification; P450 61

9/3,K/27 (Item 1 from file: 73) Links

Fulltext available through: STIC Full Text Retrieval Options

EMBASE

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0081088163 EMBASE No: 2006148259

Sterol regulatory element binding protein is a principal regulator of anaerobic gene expression in fission yeast

Todd B.L.; Stewart E.V.; Burg J.S.; Hughes A.L.; Espenshade P.J.

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Molecular and Cellular Biology (Mol. Cell. Biol.) (United States) April 1, 2006 , 26/7 (2817-2831)

CODEN: MCEBD ISSN: 0270-7306

Item Identifier (DOI): 10.1128/MCB.26.7.2817-2831.2006

Document Type: Journal ; Article Record Type: Abstract

Language: English Summary language: English

Number of References: 38

Sterol regulatory element binding protein is a principal regulator of anaerobic gene expression in fission yeast

Fission yeast sterol regulatory element binding protein (SREBP), called Sre1p, functions in an oxygen-sensing pathway to allow adaptation to fluctuating oxygen concentrations. The Sre1p-Sc1p complex responds to oxygen-dependent sterol synthesis as an indirect measure of oxygen availability. To examine the role of Sre1p in anaerobic... ..target gene promoters and stimulates its own transcription under anaerobic conditions. sre1 SUP + promoter analysis identified two DNA elements that are both necessary and sufficient for oxygen-dependent, Sre1p-dependent transcription. Interestingly, these elements are homologous to sterol regulatory elements bound by mammalian SREBP, highlighting the evolutionary conservation between Sre1p and SREBP. We...

Drug Descriptors:

* oxygen; *sterol--endogenous compound--ec; *sterol regulatory element binding protein--endogenous compound--ec

Medical Descriptors:

* aerobic metabolism; *gene expression regulation; *Schizosaccharomyces pombe ; *sterol synthesis

article; chromatin immunoprecipitation; controlled study; DNA sequence; gel mobility shift assay; gene induction; glycolysis; immunoblotting; mitochondrial respiration; nonhuman; Northern blotting; oxidative phosphorylation; oxygen consumption; oxygen sensing; priority journal; promoter region; Saccharomyces cerevisiae; yeast

Orig. Descriptors:

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9/3,K/28 (Item 1 from file: 155) Links

Fulltext available through: STIC Full Text Retrieval Options

MEDLINE(R)

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16356471 PMID: 15855491

Candida albicans zinc cluster protein Upc2p confers resistance to antifungal drugs and is an activator of ergosterol biosynthetic genes.

MacPherson Sarah; Akache Bassel; Weber Sandra; De Deken Xavier; Raymond Martine; Turcotte Bernard
Department of Medicine, Royal Victoria Hospital, McGill University, 687 Pine Ave. West, Montreal, Quebec, Canada H3A 1A1.

Antimicrobial agents and chemotherapy (United States) May 2005 , 49 (5)

p1745-52 , ISSN: 0066-4804--Print Journal Code: 0315061

Publishing Model Print

Document type: Journal Article; Research Support, Non-U.S. Gov't

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

...often due to an increase in drug efflux or an alteration of the pathway for synthesis of ergosterol, an important plasma membrane component in fungi. However, little is known about the transcription factors that mediate drug resistance. In *Saccharomyces cerevisiae*, two highly related transcriptional activators, Upc2p and Ecm22p, positively regulate the expression of genes involved in ergosterol synthesis (ERG genes). We have identified a homologue in *C. albicans* of the *S. cerevisiae* UPC2/ECM22 genes and named it UPC2. Deletion of this gene impaired growth under anaerobic... remained unchanged. Importantly, the purified DNA binding domain of Upc2p bound in vitro to putative sterol response elements in the ERG2 promoter, suggesting that Upc2p increases the expression of the ERG... (

Descriptors: *Antifungal Agents--pharmacology--PD; *Candida albicans--drug effects--DE; *Candida albicans--genetics--GE; *Ergosterol--biosynthesis--BI; *Ergosterol--genetics--GE; *Saccharomyces cerevisiae Proteins --metabolism--ME; *Trans-Activators--metabolism--ME ; ...Azoles--pharmacology--PD; Blotting, Northern; Blotting, Southern; Culture Media; Drug Resistance, Fungal; Electrophoretic Mobility Shift Assay; Fungal Proteins--biosynthesis--BI; Microbial Sensitivity Tests; Molecular Sequence Data; Plasmids--genetics--GE; Promoter Regions (Genetics)--genetics--GE; RNA, Fungal--biosynthesis --BI; RNA, Messenger--biosynthesis--BI; Saccharomyces cerevisiae--genetics--GE; Saccharomyces cerevisiae --metabolism--ME

Named Person:

Chemical Name: Antifungal Agents; Azoles; Culture Media; Fungal Proteins; RNA, Fungal; RNA, Messenger; Saccharomyces cerevisiae Proteins; Trans-Activators; UPC2 protein, *S. cerevisiae*; Ergosterol

9/3,K/29 (Item 1 from file: 393) Links

Beilstein Database - Abstracts

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Beilstein Abstract Id: 6494909

Title: Genomic Approach to Identification of Mutations Affecting Caspofungin Susceptibility in *Saccharomyces cerevisiae*

Document Type: Journal Record Type: Abstract

Author: Markovich, Sarit; Yekutieli, Aya; Shalit, Itamar; Shadkchan, Yona; Osherov, Nir

Citation: Antimicrob. Agents & Chemother. (2004) Series: 48-10, 3871 - 3876 CODEN:

AMACQ Language: English

Abstract Language: English

Title: Genomic Approach to Identification of Mutations Affecting Caspofungin Susceptibility in *Saccharomyces cerevisiae*

Document Type:

Abstract: The antifungal agent caspofungin (CAS) specifically interferes with glucan synthesis and cell wall formation. To further study the cellular processes affected by CAS, we analyzed a *Saccharomyces cerevisiae* mutant collection (4,787 individual

sterolbiosynthesis.txt

knockout mutations) to identify new genes affecting susceptibility to the drug. This collection was screened for increased CAS sensitivity (CAS-IS) or increased CAS resistance (CAS-IR). MICs were determined... the protein kinase C (PKC) integrity pathway (MID2, FKS1, SMI1, and BCK1), chitin and mannan biosynthesis (CHS3, CHS4, CHS7, and MNN10), and ergosterol biosynthesis (ERG5 and ERG6). Four of the 20 genes (TPO1, VPS65, VPS25, and CHC1) are involved... staurosporine in combination with CAS was tested against eight *Aspergillus* clinical isolates by the microdilution assay. Synergistic or synergistic-to-additive activities were found against all eight isolates by use of...

Abstract Language:

9/3,K/30 (Item 2 from file: 393) Links

Beilstein Database - Abstracts

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Beilstein Abstract Id: 6456504

Title: Pyridines and Pyrimidines Mediating Activity against an Efflux-Negative Strain of *Candida albicans* through Putative Inhibition of Lanosterol Demethylase

Document Type: Journal Record Type: Abstract

Author: Buurman, Ed T.; Blodgett, April E.; Hull, Kenneth G.; Carcanague, Daniel

Citation: Antimicrob. Agents & Chemother. (2004) Series: 48-1, 313 - 318 CODEN:

AMACCQ Language: English

Abstract Language: English

Title: ... Pyrimidines Mediating Activity against an Efflux-Negative Strain of *Candida albicans* through Putative Inhibition of Lanosterol Demethylase

Document Type:

Abstract: The first step in ergosterol biosynthesis in *Saccharomyces cerevisiae* consists of the condensation of two acetyl coenzyme A (acetyl-CoA) moieties by acetoacetyl-CoA thiolase, encoded by ERG10. The inhibition of the sterol pathway results in feedback activation of ERG10 transcription. A cell-based reporter assay, in which increased ERG10 transcription results in elevated specific beta-galactosidase activity, was used to find novel inhibitors of ergosterol biosynthesis that could serve as chemical starting points for the development of novel antifungal agents. A class of pyridines and pyrimidines identified in this way had no detectable activity against the major fungal pathogen *Candida albicans* (MICs... ml⁻¹), suggesting that they are efficiently removed from wild-type cells. Quantitative analysis of sterol intermediates that accumulated during growth inhibition revealed the accumulation of lanosterol at the expense of ergosterol. Furthermore, a clear correlation was found between the 50 percent inhibitory concentration at which the sterol profile was altered and the antifungal activity, measured as the MIC. This finding strongly suggests that the inhibition of growth was caused by a reduction in ergosterol synthesis. The compounds described here are a novel class of antifungal pyridines and pyrimidines and the... mi)dines to be shown to putatively mediate their antifungal activity against *C. albicans* via lanosterol demethylase.

Abstract Language:

9/3,K/31 (Item 1 from file: 35) Links

Dissertation Abs Online

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01952262 ORDER NO: AADAA-I3090202

Molecular biological approaches to biomedical problems in sterol and terpene biosynthesis

Author: Xu, Ran

Degree: Ph.D.

Year: 2003

Corporate Source/Institution: Rice University (0187)

Source: Volume 6405B of Dissertations Abstracts International.

PAGE 2182 . 129 PAGES

Molecular biological approaches to biomedical problems in sterol and terpene biosynthesis

...wide variety of biomedical problems. Described herein is the use of metabolic engineering to manipulate sterol biosynthesis for medicinal purposes. Also presented is the cloning of terpene biosynthetic genes in plants of agricultural and pharmacological importance.

Two examples of metabolic engineering of the *Saccharomyces cerevisiae* sterol biosynthetic pathway are illustrated in Part I. We first demonstrated the development of genetically engineered *S. cerevisiae* strains that efficiently produce meiosis activating sterols (MAS), which are difficult to obtain by chemical synthesis or isolation from natural sources. Homologous recombination was used to construct an *erg24*Δ... in vivo MAS production needs no added substrate, is technically simpler than chemical synthesis, and provides an inexhaustible source of MAS in relatively high purity and yield. In a different approach to metabolic engineering, we generated recombinant *S. cerevisiae* strains to screen drugs against the pathogenic parasite *Trypanosoma cruzi*. The native sterol Δ⁸-Δ⁷ isomerase in *S. cerevisiae* was replaced by the heterologous *T. cruzi* sterol isomerase and the corresponding human enzyme respectively. The relative effectiveness of the tested compounds on these two strains was compared using simple plate assay and validated by chromatographic methods. This differential screening method identifies inhibitors that specifically target the *T. cruzi* sterol isomerase with minimal side-effect on the parallel human enzyme and avoids the direct handling... uncovered from *M. truncatula* Expressed Sequence Tag libraries was expressed in *S. cerevisiae*, and the recombinant enzyme cyclized 2,3-oxidosqualene cleanly into β-amyrin. Also, a...

9/3,K/32 (Item 2 from file: 35) Links

Dissertation Abs Online

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01861281 ORDER NO: AADAA-I3032438

Characterization of the membrane associated progesterone receptor (MAPR) homologues in *Saccharomyces cerevisiae* and *Arabidopsis thaliana*

Author: Gray, Phillip Neal

Degree: Ph.D.

Year: 2001

Corporate Source/Institution: Georgia Institute of Technology (0078)

Source: Volume 6211B of Dissertations Abstracts International.

PAGE 4944 . 80 PAGES

ISBN: 0-493-44909-4

Characterization of the membrane associated progesterone receptor (MAPR) homologues in *Saccharomyces cerevisiae* and *Arabidopsis thaliana*

...MAPR) family is highly conserved among eukaryotes. Here we report the characterization of the *Saccharomyces cerevisiae* MAPR homologue YPL170w, which we have named EPA1, for Ergosterol Precursor Accumulating. The null mutant... prolonged lag in growth when exposed to the fusel alcohols isoamyl and active amyl alcohol. Sterol analysis of *epa1*Δ revealed this mutant accumulates high levels of ergosterol precursors... control. Over-expression of *Epa1* in *epa1*Δ cells nearly restores wild type sterol levels. Both control and *epa1*Δ cells recovering from isoamyl alcohol show similar alterations in their sterol profiles, suggesting that modification of sterol composition may be involved in adaptation to isoamyl alcohol. *Epa1*-GFP fusions localize to lipid particles, which are known sites of sterol storage and biosynthesis. These data suggest a role in sterol metabolism for *Epa1*, and possibly for MAPR homologues in plants and mammals.

I used EPA1 as bait in a yeast two-hybrid screening and isolated an uncharacterized gene, YPR118w. YPR118w possesses a conserved domain found in the eIF2B... *ypr118w*Δ/*epa1*Δ behaves similar to *epa1*Δ. Sterol profiles of *ypr118w*Δ appear similar to controls, whereas

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<italic>ypr118wΔ</italic>... The <italic>Arabidopsis thaliana</italic> MAPK homologue Atmp1 was also characterized by yeast two-hybrid assay, sequence analysis and GUS assay. The two-hybrid screening resulted in the identification of two uncharacterized genes, which were designated At15 and At69. EST database searches for Atmp1...

9/3,K/33 (Item 3 from file: 35) Links

Dissertation Abs Online

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01803353 ORDER NO: AADAA-I9940801

THE SEARCH FOR TRANS- AND CIS-ACTING DETERMINANTS OF SACCHAROMYCES CEREVISIAE MOD5P SUBCELLULAR DISTRIBUTION (PROTEIN SORTING, NONSENSE SUPPRESSION, NUCLEAR LOCALIZATION)

Author: BENKO, ANN LYNN

Degree: PH.D.

Year: 1999

Corporate Source/Institution: THE PENNSYLVANIA STATE UNIVERSITY (0176)

Source: Volume 6008B of Dissertations Abstracts International.

PAGE 3731 . 188 PAGES

THE SEARCH FOR TRANS- AND CIS-ACTING DETERMINANTS OF SACCHAROMYCES CEREVISIAE MOD5P SUBCELLULAR DISTRIBUTION (PROTEIN SORTING, NONSENSE SUPPRESSION, NUCLEAR LOCALIZATION)

The <italic>S. cerevisiae</italic> sorting isozyme, Mod5p, which catalyzes tRNA isopentenylation, has two known isoforms: Mod5p-I, present... and cytosol, and Mod5p-II, located in the nucleus and cytosol. In an attempt to identify genes of cytosolic factors involved in delivery of Mod5p-I to the mitochondria, yeast containing... act as sorting factors. YDL219w and <italic>TEF4</italic> products also probably participated in protein synthesis. Cells overexpressing <italic>ERG20</italic> had 70% less isopentenyl tRNA than control cells. Since Erg20p... Mod5p-I sorting factors were probably not found, the selection of Erg20p suggests that this assay might be used to monitor sterol synthesis pathway flux, perhaps beneficial to drug development.

In a search for a nuclear localization signal...

9/3,K/34 (Item 1 from file: 135) Links

NewsRx Weekly Reports

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0000317793 (USE FORMAT 7 OR 9 FOR FULLTEXT)

Researchers' findings from the United States and Canada advance cancer treatment research

Cancer Gene Therapy Week, July 17, 2006, p.60

DOCUMENT TYPE: Expanded Reporting LANGUAGE: English

RECORD TYPE: FULLTEXT

Word Count:

997

... proliferation of activated T cells and augmentation of allogeneic T cell generation in an MLR assay.

"Purified GPI-hIL-12 was efficiently intercalated onto isolated tumor cell membrane vesicles prepared from...

sterolbiosynthesis.txt

...with tumorigenesis often include loss of cell cycle checkpoints or alteration in growth signaling pathways. Identification of novel genes involved in cellular proliferation may lead to new classes of cancer therapeutics," scientists in the United States reported.

"By screening a tetracycline-inducible cDNA library in A549 cells for genes that interfere with proliferation, we have identified a fragment of UHRF1, a nuclear RING finger protein, that acts as a dominant negative...

...of ubiquitin E3 ligases."

The scientists announced, "We have confirmed using an in vitro autoubiquitination assay that UHRF1 displays RING-dependent E3 ligase activity. Overexpression of a GFP-fused UHRF1 RING...

...anticancer lysophospholipid.

"Edelfosine is a prototypical member of the alkylphosphocholine class of antitumor drugs. *Saccharomyces cerevisiae* was used to screen for genes that modulate edelfosine cytotoxicity and identified sterol and sphingolipid pathways as relevant regulators. Edelfosine addition to yeast resulted in the selective partitioning...

...plasma membrane to intracellular punctate regions and finally localized to the vacuole. Consistent with altered sterol and sphingolipid synthesis resulting in increased edelfosine sensitivity, mislocalization of Pma1p was preceded by the movement of sterols...

9/3,K/35 (Item 1 from file: 357) Links

Derwent Biotech Res.

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0363185 DBA Accession No.: 2005-08889 PATENT

Determining whether molecule affects sterol biosynthesis pathway activity in *Saccharomyces cerevisiae* cell, based on change in RNA expression of marker gene linked to *Saccharomyces* gene promoter, in cell in presence/absence of molecule sterol production via fungus cell culture for use in disease therapy

Author: PHILLIPS J W

Patent Assignee: ROSETTA INPHARMATICS LLC 2005

Patent Number: WO 200512559 Patent Date: 20050210 WPI Accession No.: 2005-152458 (200516)

Priority Application Number: US 491442 Application Date: 20030730

National Application Number: WO 2004US24034 Application Date: 20040726

Language: English

Determining whether molecule affects sterol biosynthesis pathway activity in *Saccharomyces cerevisiae* cell, based on change in RNA expression of marker gene linked to *Saccharomyces* gene promoter, in cell in presence/absence of molecule sterol production via fungus cell culture for use in disease therapy

Abstract: DERWENT ABSTRACT: NOVELTY - Determining (M1) whether a molecule affects sterol biosynthesis pathway activity in *Saccharomyces cerevisiae* cell, comprising contacting cell with the molecule, and determining affect of molecule on activity of... ..absence of molecule, where target polynucleotide is a sequence linked to promoter native to *S. cerevisiae* gene YMR325W, is new. DETAILED DESCRIPTION - Determining (M1) whether a molecule affects the function or activity of a sterol biosynthesis pathway in *Saccharomyces cerevisiae* cell, or determining the effect of a molecule upon the function or activity of a sterol biosynthesis pathway, comprising: (a) contacting the cell with, or recombinantly expressing within the cell, the molecule... ..where the target polynucleotide is a sequence operatively linked to a promoter native to *S.cerevisiae* gene YMR325W, or their homologs; or detecting a change in RNA or protein expression in... ..the molecule, where the target polynucleotide sequence is regulated by a promoter native to *S.cerevisiae*

YMR325W gene, or their homologs; and (c) determining that the molecule affects the function or activity of the sterol biosynthesis pathway if expression of the target polynucleotide is changed, or determining that the molecule does not affect the function or activity of the sterol biosynthesis pathway if expression of the target polynucleotide sequence is unchanged; or determining the affect of the molecule upon the function or activity of the sterol biosynthesis pathway based upon the change in RNA or protein expression. INDEPENDENT CLAIMS are also included for: (1) monitoring (M2) activity of a sterol biosynthesis pathway in a *S.cerevisiae* cell exposed to a molecule, comprising: (a) contacting the cell with, or recombinantly expressing within... ..the molecule, where the target polynucleotide sequence is regulated by a promoter native to *S.cerevisiae* gene YMR325W, or their homologs, and (c) determining that the activity of the sterol biosynthesis pathway in the cell is changed if expression of the target polynucleotide is determining to be changed in step (b), or determining that the activity of the sterol biosynthesis pathway in the cell is unchanged if expression of the target polynucleotide is determined to be unchanged in step (b); (2) identifying (M3) a molecule that modulates expression of a sterol biosynthesis pathway target polynucleotide sequence, involves recombinant expression in *S.cerevisiae* cell, or contacting *S.cerevisiae* cell with, one or more candidate molecules, and measuring RNA or protein expression in the... ..a target polynucleotide sequence which is a sequence regulated by a promoter native to *S.cerevisiae* YMR325W gene, or their homologs, where an increase or decrease in expression of the target... ..in the absence of the candidate molecule indicates that the candidate molecules expression of the sterol biosynthesis pathway target polynucleotide sequence; and (3) determining whether a first *S. cerevisiae* cell is mutant for a sterol biosynthesis pathway gene, comprising: (a) in the first *S.cerevisiae* cell, determining the RNA or protein expression of a target polynucleotide sequence, which is a sequence regulated by a promoter native to a *S. cerevisiae* YMR325W gene, or their homologs, where the cell is not being exposed to an inhibitor of a sterol biosynthesis pathway; (b) determining whether the RNA and/or protein expression of the target polynucleotide sequence... ..the RNA and/or protein expression of the target polynucleotide sequence in a second *S.cerevisiae* cell which is believed to be wild-type for sterol biosynthesis genes; and (c) determining that the *S. cerevisiae* cell is mutant for a sterol biosynthesis pathway gene if expression of the target polynucleotide sequence is determined to be changed in step (a), or determining that the first *S. cerevisiae* cell is not mutant for a sterol biosynthesis pathway gene if expression of the target polynucleotide sequence is determined to be unchanged in step (b). WIDER DISCLOSURE - A pharmaceutical composition comprising the molecules identified by (M3), to treat fungal infections or hypercholesterolemia. BIOTECHNOLOGY - Preferred Method: In (M1), the target... ..The step (c) involves determining that the molecule affects the function or activity of the sterol biosynthesis pathway if expression of the marker gene is changed, or determining that the molecule does not affect the function or activity of the sterol biosynthesis pathway if expression of the marker gene is unchanged. The step of determining whether the molecule inhibits sterol biosynthesis, involves determining whether the cell contacted with the molecule exhibits a lower level of sterol than a second cell, which is not contacted with the molecule. The step (b) involves... ..or protein expression is changed. (M1) is a method for determining whether the molecule inhibits sterol biosynthesis, which involves the step (c) of determining that the molecule inhibits sterol biosynthesis if expression of the target polynucleotide sequence in step (a) is increased relative to expression of the target polynucleotide sequence in the absence of the molecule. The *S. cerevisiae* cell is a cell that recombinantly expression the target polynucleotide sequence. The step (a) involves... ..the molecule, where the step (a) is carried out in a liquid high throughput-like assay, solid plate halo assay, or in an agar overlay assay. The promoter comprises a fully defined sequence of 1001 base pairs as given in the... ..that the effect of the molecule is to inhibit the function or activity of the sterol biosynthesis pathway. The step (b) involves determining that the expression is increased, and step (c) involves determining that the activity of the sterol biosynthesis pathway is inhibited. The target polynucleotide sequence comprises *S. cerevisiae* YMR325W. USE - (M1) is useful for determining whether a molecule affects the function or activity of a sterol biosynthesis pathway in *S.cerevisiae* cell, or determining the effect of a molecule upon the function or activity of a sterol biosynthesis pathway, where the molecule is chosen from natural products, proteins

sterolbiosynthesis.txt

and small molecules (claimed). (M1) is useful in screening chemical libraries and natural products for compounds that are used as antifungal agents or as...
...specificity of antifungal agents and lipid lowering agents, and/or to monitor the activity of sterol biosynthesis pathway. ADVANTAGE - (M1) enables determination of whether a molecule affects the function or activity of a sterol biosynthesis pathway in *S. cerevisiae* cell. EXAMPLE - A YMR325W gene reporter obtained from *Saccharomyces cerevisiae* was transformed into wild-type *S. cerevisiae* strain ABY12 and grown on solid Casamino acids media plates. The culture from the solid... media to an OD(600) value of 1. Drug-like agents Lovastatin, Miconazole and Fenpropimorph, sterol biosynthesis inhibitors that target different molecular steps in the sterol biosynthesis pathway, and UDP-N-acetyl-glucosamine-1-P transferase (GPT) inhibitor Tunicamycin, a negative control, were used in the assay. Each of the four drugs was added to individual wells (one drug per well) in the second column of a 96-well assay plate and serially diluted into Casamino acids media plus 2 % dimethylsulfoxide (DMSO) in columns 3... and incubated at 30 degreesC for 24 hours. After 24 hours incubation the 96-well assay plate was imaged in a Molecular Dynamics Fluorimager SI to measure the fluorescence from the... YMR325W gene reporter showed increased fluorescence when exposed to the higher concentrations of all three sterol biosynthesis inhibitors tested. No increase in fluorescence was observed for any of the concentrations of GPT... the utility of YMR325W reporter for use as a gene reporter in high-throughput liquid screens for identifying inhibitors of sterol biosynthesis. (48 pages)

E.C. Numbers:

Descriptors: recombinant sterol prep., recombinant *Saccharomyces cerevisiae* cell culture, molecule affect det., green, red, blue fluorescent protein, luciferase marker gene, gene promoter, appl. chemical library screening, lipid lowering agent, hypercholesterolemia, fungus therapy steroid alcohol fungus yeast fluorescence enzyme DNA sequence protein...

9/3,K/36 (Item 1 from file: 8) Links

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Ei Compendex(R)

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07843103 E.I. No: EIP97103857095

Title: Sterol Delta14 reductase screen

Author: Lai, Margaret H.K.; Kirsch, Donald R.; Bard, Martin E.

Corporate Source: American Cyanamid Co, Brunswick, NJ, USA

Source: Biotechnology Advances v 15 n 3-4 1997. p 709

Publication Year: 1997

CODEN: BIADDD ISSN: 0734-9750

Language: English

Title: Sterol Delta14 reductase screen

Abstract: A binary assay identifies agents that inhibit sterol Delta14 reductase involved in ergosterol biosynthesis. In the primary screen, sterol Delta14 reductase inhibition by a test sample is assayed by adding the test sample to... 1 mutation, comparing the extent of growth inhibition after incubation in the two cultures, and identifying as positives those samples that show growth inhibition in the erg-3 culture exceeding that in the erg-1 culture. In the secondary screen, samples that test positive in the primary screen are reassayed by adding the test sample to a culture of a *Saccharomyces cerevisiae* strain into which has been introduced multiple copies of a gene encoding sterol Delta14 reductase and also to a strain of *S. cerevisiae* that does not have the introduced gene; positive samples are identified after incubation by observation that growth inhibition in the culture having no introduced reductase gene... in the culture having the introduced reductase gene. In preferred embodiments, a known inhibitor of sterol Delta14 reductase is employed in solidified media in both the primary and the secondary screens, resulting in an assay that is highly sensitive and specific for the detection of sterol Delta14 reductase inhibitors. (Author abstract)

Descriptors: *Enzyme inhibition; Bioassay; Biosynthesis; Cell culture; Genetic engineering; Mutagenesis

Identifiers: Sterol Delta14 reductase; Abstract only
Identifiers:

9/3,K/37 (Item 1 from file: 149) Links
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01085203 Supplier Number: 03663163 (USE FORMAT 7 OR 9 FOR FULL TEXT)
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Cruickshank, Alexander M.
Science , V227 , p1067(38)
March 1 ,
1985
Publication Format: Magazine/Journal
ISSN: 0036-8075
Language: English
Record Type: Fulltext Target Audience: Academic
Word Count: 27162 Line Count: 03286

...catabolism of acetogens'; Eva R. Kashket, "Proton motive force and bacterial metabolism.' Novel products of biosynthesis (Douglas E. Everleigh, discussion leader): Hamish McArthur, "Biosynthesis of industrially important microbial exopolysaccharides'; Burt D. Ensley, "Genetic manipulation of metabolic operons for new...

...Crawford, discussion leader): T. Kent Kirk, "Lignin-degrading enzymes'; D. W. S. Westlake, "Cell-free synthesis of B-lactam antibiotics in streptomyces clavuligerus'; J. Oliver Lampen, "Exoenzyme secretion in bacillus.' Enzyme...Andrew Vasella, "1-Deoxy-1-nitroaldoses and related compounds'; William R. Roush, "Studies in carbohydrate synthesis.' (Paul A. Sandford, discussion leader): Alan Darvill, "Plant cell-wall polysaccharides and biologically active oligosaccharides...

...Hans Paulsen, "Problems in oligosaccharide syntheses'; C. D. Warren, "Application of synthetic intermediates to glycoprotein biosynthesis .' (Annette Herscovics, discussion leader): Frank Maley, "The use of endoglycosidases in clarifying the structure and...

...vessel function.'
28 June. (Andrea Vasella, discussion leader): G. W. J. Fleet, "Approaches to the synthesis of alkaloids from carbohydrates'; Richard L. Tolman, "Carbohydrate derivatives in the synthesis of acyclonucleoside substrates for herpes thymidine kinase.'
CO2 Fixation by Green Plants
Kimball Union Academy...

...Light inducible nuclear genes encoding chloroplast proteins'; K. Keegstra, "Role of chloroplast envelope in protein synthesis'; G. W. Schmidt, "Post-translational modification M. Shibbles, discussion leader): G. D. Ogren, discussion leader...

...metal complexes as oxidation catalysts'; Younes Ben Taarit, "Rhodium and iridium carbonyl compounds in zeolites: Synthesis, characterization and catalytic properties in CO reactions'; Joe Hightower and Geoffrey Price, "Te-NaX zeolites...catalysis of rhodium metal in syngas conversion to oxygenates'; Vladimir Ponec, "Rhodium catalysts for the synthesis of oxygenates; the function of cations.'
27 June. Duward Shriver, "Ensemble effects in organometallic CO...

...Proctor Academy
Barry Hoffer, chairman; David C. Klain, vice chairman.

29 July. Regulation of catecholamine synthesis, storage and release: Molecular aspects (Norman Weiner, session chairman): Norman Weiner, "Regulation of tyrosine hydroxylase...

...session chairman): David Sugden, "Adrenergic control of cyclic nucleotides"; Pierre Voissin, "Adrenergic control of protein synthesis"; Richard Zigmond, "Phospholipid regulation"; David Klein, "Adrenergic control of indoleamine synthesis." Peptides as catecholamine co-transmitters (Bertil Fredholm, session chairman): Bertil Fredholm, "Overview"; David Jacobowitz, "Anatomical...in and physical aging of polymeric glasses." (J. O. Stoffer, discussion leader): J. E. McGrath, "Synthesis and characterization of functionally reactive polymers"; C. E. Hoyle, "Photodegradation of aromatic diisocyanate based polyurethanes ...H. F. Schaake, "Solid-state recrystallization and LPE of HgCdTe"; R. C. Pastor, "Low-temperature synthesis of high-temperature compounds."

Developmental Biology

Proctor Academy

Allan Spradling, chairman; Robert Horvitz, vice chairman...of metabolites"; David Garcia, "Robotics in the study of drug metabolism as applied to complex assay methodology."

Dynamics of Gas-Surface Interactions

Colby-Sawyer College (S)

J. C. Tully, chairman; S...

...elastin gene"; Savio Woo, "Structure and expression of the 1 antiprotease gene." Regulation of elastin biosynthesis (Jeffrey Davidson, discussion leader): J. Davidson, "Developmental regulation of elastin synthesis"; R. P. Mecham, "Hormonal and matrix influences on elastin metabolism"; Discussants: C. Franzblau, C. Boyd...

...for the improvement of rolling resistance of butadiene rubbers"; Ph. Teyssie, "Further developments in the synthesis of block copolymers and their applications to emulsions and blends." (A. Y. Coran, discussion leader...R. Kaback, "Lac permease."

3 July. (L. Ernster, discussion leader): Y. Hatefi, "Mechanism of ATP synthesis probed with inhibitors"; W. Sebald, "Structure of the proton channel"; G. Cox, "Genetic studies on...

...J. Oppenheimer, co-vice chairman.

8 July. (P. A. Bartlett, session chairman): A. R. Battersby, "Biosynthesis of the pigments of life"; H. G. Floss, "Biosynthesis of some microbial natural products"; S. J. Gould, "Recent discoveries in antibiotic biosynthesis"; R. J. Parry, "Recent investigations of the biosynthesis of nitrogen-containing natural products." (J. Stubbe...

...H. G. Wood, "The central role of the nickel enzyme, CO dehydrogenase, in the autotrophic synthesis of acetate"; C. T. Walsh, "Nickel-dependent enzymes in the biogenesis of natural gas."

9...

...P. R. Schimmel, "Selecting for mutations which give higher catalytic power"; S. M. Hecht, "Protein biosynthesis with misacylated tRNA's"; J. Ofengan, "tRNA-ribosome interactions."

11 July. (R. G. Matthews, session...the two phase acrosome reaction in sperm of marine shrimp."

15 August. Control of protein synthesis and messenger RNA utilization in oocyte and egg activation (Merrill Hille, discussion leader): James Maller...in the synthesis of natural products." (J. Wilt, discussion leader): H. Viehe, "Captodative radicals in synthesis."

12 June. (R. Neuman, discussion leader): W. Adam, "Laser photochemical generation of diradicals"; M. Paddon...

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...of free radicals.' (R. Neuman, discussion leader): D. Hart, "Free radical cyclizations in natural product synthesis"; D. Little, "Diyl trapping reactions."

13 June. (D. Griller, discussion leader): G. Russell, "Nucleophilic substitution...Vernon Reinhold, "Oligosaccharide processing: Molecular characterization"; Rosalind Kornfeld, "Characterization of an ER-mannosidase";

Paul Atkinson, "Synthesis and processing of rotavirus glycoproteins in the rough endoplasmic reticulum." (Akira Kobata, discussion leader): Dirk van den Eijnden, "Biosynthesis of polylactosaminoglycans: Initiation, elongation, branching and terminations"; Carlos Hirschberg, "Mechanisms of glycosylation in the golgi ...

...Multiple pathways utilizing coated vesicles for transport of macromolecules.' (Stuart Kornfeld, discussion leader): Stuart Kornfeld, "Identification of a second man-6-P receptor"; Martin Snider, "Transport of cell surfaces glycoproteins to...
...acetylactosamine sequences on tumor cell glycoproteins and metastasis." Phillip Robbins, "Yeast mutants in cell wall synthesis"; Peter Albersheim, "Rhizobium polysaccharides: Do they function in symbiosis?"

29 August. (Nathan Sharon, discussion leader...

...and homologies of human, rat and mouse.'

30 August. (Charles Sweeley, discussion leader): Subhash Basu, "Biosynthesis of blood group-active glycosphingolipids"; Glyn Dawson, "Regulation of glycolipid synthesis in neural tissue"; Yoshitaka Nagai, "Induction of disialganglioside GD3 in rat cultured cells by the...
New Hampton School

Peter Beak, chairman; Ronald Gammill, vice chairman.

8-12 July. H. Alper, "Synthesis and chemistry of heterocycles via transition metal catalysis"; A. G. M. Barrett, "Recent advances in...

...Heckendorn, "Novel heterocycles by the malonic ester variation of the Japp-Klingemann reaction"; A. Holmes, "Synthesis of naturally occurring oxygen heterocycles"; C. R. Johnson, "Unnatural heterocycles and vice versa"; I. Lantos, "Dihydroisoquinoline ring expansions"; L. Lee, "Synthesis of heterocycles from 3-aminoacrylates"; D. Liotta, "Synthesis and reactivity of oxygenated heterocycles"; B. H. Lipshutz, "Heterocycles as intermediates in organic synthesis"; D. Powell, "A new, efficient regio-selective synthesis of aryl-2-chloropyridines"; J. Sanchez, "Synthetic studies of naphtharidines"; R. R. Schmidt, "Directed lithiation of functionally substituted vinylic compounds-- versatile intermediates in heterocyclic synthesis"; I. Shinkai, "Stereo-controlled synthesis of new 1-methylcarbapenem antibiotics"; V. Snieckus, "Amide metalation tactics for heterocyclic synthesis."

It will be possible for participants to present posters during the conference.

Hormonal Carcinogenesis
New...

...Soto, "Role of estrogens in cell proliferation"; George M. Stancel, "Estrogen control of uterine DNA synthesis"; Jack Gorski, "Role of estrogen receptors in cell proliferation." (Pentti K. Siiteri, discussion leader): Erlio...regulation of specific protein phosphorylation."
7 August. Hormones and cancer (Benita Katzenellenbogen, chairman): M. Rechler, "Biosynthesis and action of the IGF's"; K. Gabbay, "Cloning the IGF-I gene"; G. Todaro...complexes." (C. McCormack, discussion leader): C. Martin, "Luminescence probe studies of ionomers"; J. E. McGrath, "Synthesis of ionomers."

6 August. (S. R. Turner, discussion leader): J. P. Kennedy, "Synthesis of polyisobutylene-based sulfonate ionomers"; G. Wilkes,

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"Structure and properties of polyisobutylene-based sulfonated ionomers"; R. W. Lenz, "Synthesis of sulfate halato-telechelic ionomers." (R. J. Powell, discussion leader): Poster session. M. M. Coleman, "Spectroscopic studies of ion clustering in solution."

7 August. (M. Pineri, discussion leader): R. Jerome, "Synthesis of halato-telechelics"; C. Williams, "Morphology of halato-telechelics"; J. M. D. Coey, "Magnetic measurements..."

...Schachter, "Lipid fluidity of the individual hemileaflets of human erythrocyte membranes"; Daniel Friend, "Cholesterol (polyene-sterol)

localization in natural membranes.' Lipid metabolism/ enzymology, session I (Dennis Vance, chairman): Patrick Choy, "Regulation of phosphatidylcholine biosynthesis in mammalian hearts"; Ki-Han Kim, "Regulation of fatty acid synthesis"; George Carman, "Phospholipid biosynthesis in *Saccharomyces cerevisiae*"; Chris Raetz, "Genetic analysis of CDPDG metabolism in *E. coli*."

18 June. Lipid metabolism/enzymology...

...van den Bosch, "The Cerebro-Hepato-Renal (Zellweger) Syndrome: An inborn error of ether lipid biosynthesis.' Liposomes (John Weinstein, chairman): Carl Alving, "Antibodies to phospholipids, lipid bilayers, and liposomes"; Andrew Janoff, "Liposomes"; J. A. Litster, "Structure and x-ray scattering from micellar liquid crystals." H. Ringsdorf, "Synthesis, structure and properties of liquid crystalline polymers."

28 June. L. Luz, "NMR studies of discotic..."

...fat pad (Satyabrata Nandi, chairman): Stuart Smith, "Lipogenesis in mammary gland"; Pentti K. Siiteri, "Estrogen biosynthesis in adipocytes"; Bruce M. Spiegelman, "Differentiation of adipocytes."

25 June. Oncogenes and mammary tumors (Mariano...enzyme.)

27 June. Epithelial cell polarity (Ian Mather, chairman): G. Parry, "Protein secretions and membrane synthesis in cultured mammary epithelial cells"; W.

Guiseppe Inesi, chairman; Stephen G. epithelial cells'; J.-P...

...in vivo.' Atrial peptides with important biological actions (Edward H. Blain, chairman): Mary Anna Napier, "Identification and characterization of specific high affinity receptors for atrial natriuretic peptides"; Phillip Needleman, "Pharmacological characterization... mechanisms by which proteins are inserted into, and fold up correctly in, a membrane during biosynthesis, and how proteins are secreted through membranes.' Transport and sorting mechanisms (Marilyn Farquhar and William ...and welcome (John J. Partridge, chairman): Philip D. Magnus, "A progress report on the total synthesis of the dimeric indole alkaloid, vinblastine"; Robert A. Volkmann, "Boron trifluoride-activated imines in pharmaceutical chemistry"; Bruce A. Pearlman, "A new method for the synthesis of olefins from sulfones and its application to 9-deoxo-9-methylene-16, 16-dimethylprostaglandin E2 (Meteneprost)"; A. Richard Chamberlin, "Stereoselective reactions from a new synthesis of erythronolide A seco acid."

23 July. Martin Demuth, "Total synthesis of natural products: Applications of light-induced reactions"; Amos B. Smith III, "Total synthesis of the latrunculins and other architecturally novel natural products"; Kenner C. Rice, "Chiral opioid total synthesis in the study of structure and function of the opioid receptor-endorphin system."

24 July. John W. Westly, "Polyether antibiotic structure and biosynthesis"; Kyriacos C. Nicolaou, "Total synthesis of polyether antibiotics"; Rolf Scheffold, "Vitamin B12-mediated electrosynthesis of natural products"; Richard H. Schlessinger...

...aldehydes.'

25 July. Pat N. Confalone, "Intramolecular (3 2) dipolar addition reactions and the total synthesis of natural products'; Yasufumi Ohfuné, "Synthetic studies on the macrocyclic peptide antibiotic, echinocandin C'; Bruce...M. Ptashne, "Repressor-operator interaction'; K. Yamamoto, "Hormonal control of gene expression.'

13 June. Protein synthesis (H. Noller, discussion leader): M. Yarus, "Translational function of tRNA'; P. Walter, "Transport of peptide ...

...DNA technology: Status and prospects.'

19 July. P. A. Aristoff, "Intramolecular Wittig reactions in the synthesis of prostacyclin analogs'; W. D. Wulff, "Transition metal carbene complexes in organic syntheses.'

Poster sessions...

...be announced): L. S. Liebeskind, "Transformations of stoichiometric transition metal compounds of use in organic synthesis'; A. Yamamoto (subject to be announced). (Discussion leader to be announced): J. E. Lyons, "Recent reactions in organometallic chemistry'; H. E. Bryndza, "The synthesis and reactivity of metal-oxygen and metal-nitrogen bonds of group 8 metals.'

Origin of...

...the outer solar system.' (James Ferris, discussion leader): Stanley Miller, "Current status of the prebiotic synthesis of small molecules'; Eric Herbst, "Gas phase production of complex molecules in interstellar clouds.'

20...

...record of early evolution'; George E. Fox, "Molecular phylogeny'; John Olson, "The origin of photo-synthesis.' (Harold P. Klein, discussion leader): David Desmarais, "Carbon isotopes biogeochemistry of cyanobacterial mats and stromatolites...

...studies in human filariasis.' (Tony Stretton, discussion leader): Carl Johnson, "Anatomical and biochemical characterization of identified neurons in nematodes'; Martin Chalfie, "Genetic aspects of *Caenorhabditis elegans* neurons.'

30 July. (Allen Cheever...Crofts, overview speaker; bc1/b6f complexes, membrane potentials and the disposition of protons in ATP synthesis (D. Ort, W. Junge, discussion leaders). (D. Knaff, discussion leader); L. Duysens, "Biophysics in Leiden Harrington, "A general amidine synthesis via a novel 2 2 cycloaddition: Mechanistic considerations'; Thomas C. Bruice, "Oxygen insertion and addition...

...of alkali enolates'; Steve Kaiser, "Silicoalumino-phosphate molecular sieves: catalytic properties'; Harold H. Freedman, "Organic synthesis via enzymes in nonaqueous media'. (John E. Baldwin, discussion leader): Dan Farcasiu, "Super acidic strength...1 July. Polyamines and chemotherapy (J. Janne and P. Sunkara, chairmen). Molecular genetics of polyamine biosynthesis in prokaryotes and lower eukaryotes (H. Tabor and C. W. Tabor, chairmen).

2 July. Molecular genetics of polyamine biosynthesis in higher eukaryotes (P. Coffino and O. Janne, chairmen). Polyamines in parasites (P. McCann and...bacterial speciation?'; David Low, "The genetic analysis of *E. coli* that cause urinary tract infections: Identification of clonal types based on acquisition of certain chromosomal genes'; Renee Fitts, "Salmonella-specific DNA...structure of reactive polymers for organic applications'; Philip Hodge, "Novel applications of reactive polymers in synthesis'; Philip Garrou, "Study of polymer-supported catalysts under industrial conditions.' Physicochemical limitations of the polymer... ..of globin genes (David J. Weatherall, discussion leader): David J. Weatherall, "Genetic disorders of hemoglobin synthesis'; Bernard G.

Forget, "Mutations affecting the expression of the human gamma globulin genes"; Arthur Bank...

...differentiation by avian retroviral oncogenes'; Inder Verma, "Oncogenes in hematopoiesis"; George Stamatoyannopoulos, "Biology of HbF synthesis.' Membrane dynamics and erythropoiesis (Harvey Lodish, discussion leader): Elias Lazarides, "Assembly of the membrane cytoskeleton ...

...vice chairman.

8 July. Membrane formation-structure-property relationships (H. H. Hoehn, discussion leader). Membrane synthesis and preparation (C. A. Smolders, discussion leader).

9 July. Membranes for desalination (S. Sourirajan, discussion... August. (J. L. Olsen, discussion leader): D. K. Finnemore, "Proximity effect"; A. C. Motta, "Screening in proximity system"; M. Gurvitch, "Field effect and superconductivity." (J. M. Rowell, discussion leader): K. E...

...structure effects on epoxy fracture.'

30 July. (J. King, discussion leader): H. Stensenberger, "Bismaleimides: Synthesis, properties and applications"; B. Culbertson, "Bisoxazoline-phenolic resin reaction: A new route to expanding thermosetting polymers...Cohen, "Enzyme activity and toxin production.'

18 June. (W. Roush, discussion leader): W. Roush, "Synthesis of macrocyclic trichothecenes"; G. Kraus, "Synthesis analogues T-2 and DAS"; E. Colvin, "Total synthesis of deoxynivalenol.' (R. Cole, discussion leader): T. Yoshizawa, "Metabolism trichothecenes"; H. K. Kiessling, "Metabolism zearalenone.'

19...

...physiological lesion in cat.' (R. Wannemacher, Jr., discussion leader): C. S. McLoughlin, "Inhibition protein synthesis"; Y. Matsuoka, "Diarrhea induction by Fusarenone-x.'

20 June. (E. W. Sarver, discussion leader): E. V...

9/3,K/38 (Item 1 from file: 444) Links
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Medical Progress: Pneumocystis Pneumonia (Review Article)

Thomas, Charles F., Jr.; Limper, Andrew H.
The New England Journal of Medicine
Jun 10 , 2004 ; 350 (24),pp 2487-2498
Line Count: 00554 Word Count: 07655

Text:

...opportunistic infection in patients infected with the human immunodeficiency virus (HIV). (Ref. 1,2) First identified as a protozoan nearly 100 years ago and reclassified as a fungus in 1988, pneumocystis... ...an immunocompromised host. The diagnosis of pneumocystis pneumonia therefore requires microscopical examination in order to identify pneumocystis from a clinically relevant source such as specimens of sputum, bronchoalveolar fluid, or lung... ...walls and some intracystic bodies are evident. Wright-Giemsa staining can be used for rapid identification of trophic forms of the organisms within foamy exudates, as shown in Panel B (arrows... ...shown in Panel C (x400). Immunofluorescence staining, shown in Panel D, can

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sensitively and specifically identify both pneumocystis trophic forms (arrowheads) and cysts (arrows) (x400) *.**FIGURE OMITTED... ..Pneumonia

The transmission of pneumocystis is not fully understood, nor has its environmental niche been identified. For decades, the theory of the reactivation of latent pneumocystis infection -- which held that pneumocystis... ..The Biology of the Parasite

The full identification and classification of pneumocystis took many decades. Pneumocystis organisms were first identified by Carlos Chagas in the early 20th century, with the use of a guinea-pig... ..by Antonio Carinii, in infected rat lungs. (Ref. 4,5) Both investigators believed they had identified new forms of trypanosomes. Several years later, however, the Delanoes recognized that Chagas and Carinii had identified a new species with a unique tropism for the lung; hence, the new species was... ..Pneumocystis organisms have been identified in virtually every mammalian species. In humans, serologic surveys have shown nearly universal seropositivity to... ..in the setting of severe underlying immunosuppression or overwhelming infection. (Ref. 44) Microscopically, one can identify the small trophic forms (1 to 4 microm in diameter) and the larger cysts (8... ..understanding of the biology of pneumocystis in the past several years. Key molecules have been identified in the mitotic cell cycle, cell-wall assembly, signal-transduction cascades, and metabolic pathways. The... ..The first specific molecule identified from pneumocystis was a glycoprotein with an apparent molecular mass under reducing conditions of 95... ..kinase molecules homologous to those found in mating and cell-wall-integrity pathways have been identified in pneumocystis. (Ref. 68-70) The gene encoding pneumocystis mitogen-activated protein kinase (PCM) functionally complements pheromone signaling in *Saccharomyces cerevisiae*. (Ref. 70) Furthermore, the finding of enhanced activity of PCM in trophic forms as compared... ..including the putative pheromone receptors, heterotrimeric G-protein subunits, and transcription factors, have also been identified. (Ref. 74-76... ..thymidylate synthase; inosine monophosphate dehydrogenase, which is inhibited by mycophenolic acid; S-adenosyl-L-methionine:sterol C-24 methyl transferase, which is involved in the biosynthesis of sterol; and lanosterol 14(alpha)-demethylase, the target enzyme of azole antifungal compounds. (Ref. 77-80) With work on the cloning of the pneumocystis genome continuing, the identification of additional treatment targets is anticipated...

Cited References

- ...Halpern JL, Lundgren B, Swan JC, Parrillo JE, Masur H. Monoclonal antibodies to *Pneumocystis carinii*: identification of specific antigens and characterization of antigenic differences between rat and human isolates. *J Infect Dis* 1989;159:60-70.
59. Douglas CM. Fungal beta(1,3)-D-glucan synthesis. *Med Mycol* 2001;39:Suppl 1:55-66.
60. Vassallo R, Standing JE, Limper AH... ..MA, Pittarelli LA, et al. Treatment of *Pneumocystis carinii* pneumonia with 1,3-beta-glucan synthesis inhibitors. *Proc Natl Acad Sci U S A* 1990;87:5950-4.
64. Powles MA... ..Mkp1 of *Pneumocystis carinii* complements the slt2Delta defect in the cell integrity pathway of *Saccharomyces cerevisiae*. *Mol Microbiol* 1999;34:451-62.
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